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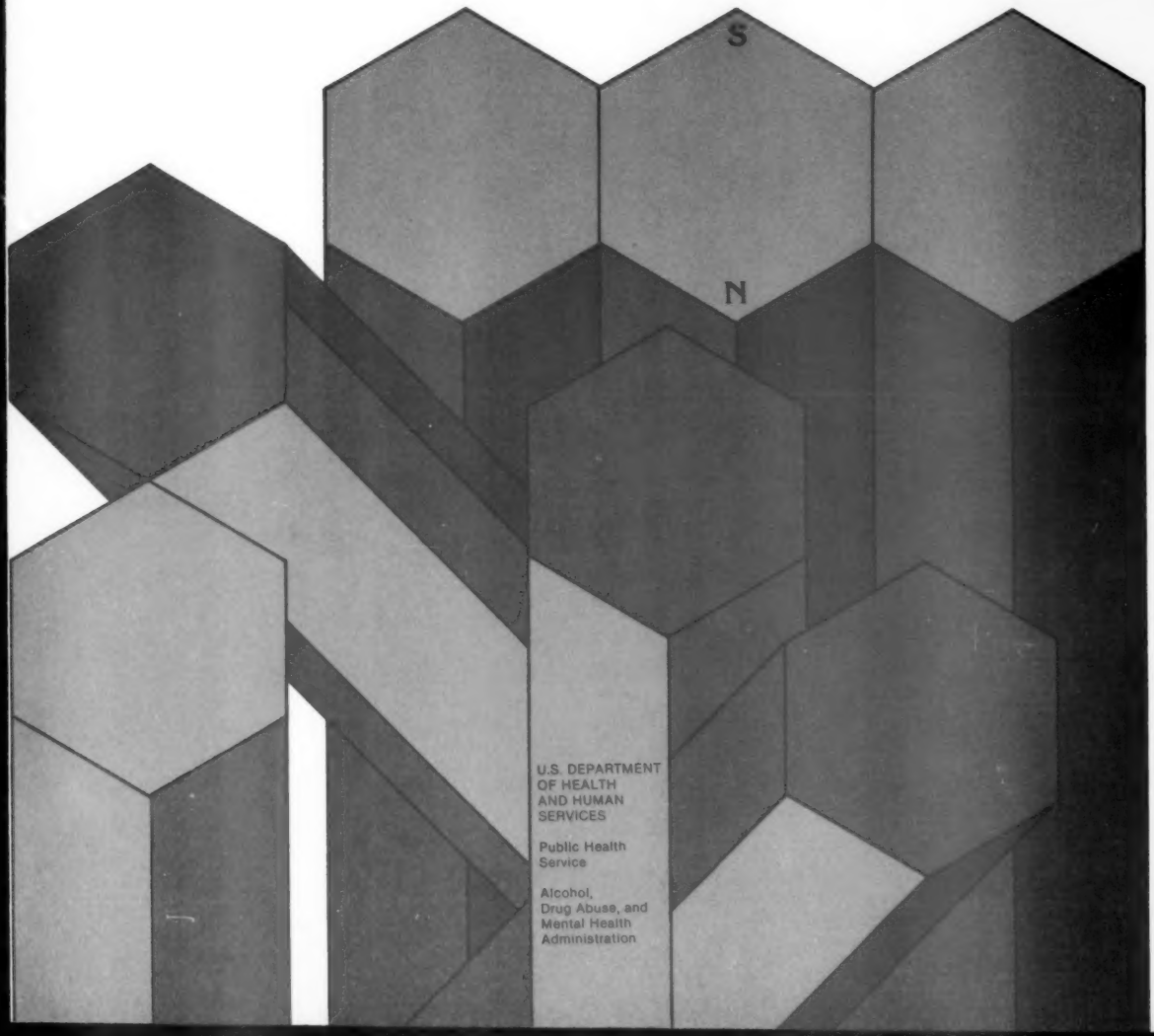

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Volume 17, Number 3 January 1980

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Carrie Lee Rothgeb, *Editor*
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ABSTRACTS

PRECLINICAL PSYCOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

001998 Clarke, Frank H.; Jaggi, Hermann; Lovell, Richard A. Research Department, Pharmaceuticals Division, CIBA-GEIGY Corporation, Ardsley, NY 10502 **Conformation of 2,9 dimethyl-3' hydroxy-5-phenyl-6,7-benzomorphan and its relation to other analgetics and enkephalin.** Journal of Medicinal Chemistry. 21-(7):600-606, 1978.

The X-ray crystallographic data for the p-bromobenzoyl ester of 2,9-dimethyl-3'-hydroxy-5phenyl-6,7-benzomorphan are presented, and the compound's structure is compared with that of morphine, meperidine, alpha-allyprodine, methadone, moramide, and enkephalins. A quantitative relationship between in vitro opiate receptor binding potency and in vivo analgesia is demonstrated for analgesics of diverse structure. A new view of the analgetic pharmacophore is presented, and programs for converting X-ray crystallographic data to rectangular coordinates with reorientation of the molecule and for calculation of torsion angles are described. (Author abstract modified)

001999 Da Re, Paolo; Valenti, Piero; Montanari, Paola; Cima, Lorenzo; Giusti, Piero. Institute of Pharmaceutical Chemistry, University of Bologna, Bologna, Italy **Neuroleptic chromone derivatives.** European Journal of Medicinal Chemistry (Paris). 13(4):387-388, 1978.

Some chromone derivatives with the characteristic features of butyrophenone neuroleptics are described. The pharmacological properties of the new compounds confirm the versatility of chromone moiety in this field of pharmaceutical chemistry. 12 references. (Author abstract)

002000 Gall, Martin; Kamdar, B. V.; Collins, R. J. CNS Diseases Research, Upjohn Company, Kalamazoo, MI 49001 **Pharmacology of some metabolites of triazolam, alprazolam, and diazepam prepared by a simple, one-step oxidation of benzodiazepines.** J ırnal of Medicinal Chemistry. 21(12):1290-1294, 1978.

A direct, one step oxidation procedure which cleanly converts diazepam, triazolobenzodiazepines such as triazolam and alprazolam, and imidazo analogue 13 to the corresponding hydroxy derivatives is described. This reaction may be used to convert diazepam to temazepam. 4-Hydroxytriazolo (4,3-a)(1,4)benzodiazipines have low central nervous system sedative and anticonvulsive activity in sharp contrast to metabolites of diazepam which remain active. While 10, an alpha-hydroxy metabolite of triazolam, retains much of the activity of 7, 10a, an alpha, 4-dihydroxy metabolite of triazolam is 250 times less potent than 7 on the nicotine antagonism assay and over 300 times less potent on the traction assay. 22 references. (Author abstract modified)

002001 Humber, Leslie G.; Sideridis, Niko; Asselin, Andre A.; Bruderlein, Francois T.; Voith, Katherine. Chemistry Department, Ayerst Research Laboratories, Montreal, Quebec, Canada H3C 3J1 **Neuroleptics related to butaclamol: an investigation of the effects of chlorine substituents on the aromatic rings.** Journal of Medicinal Chemistry. 21(12):1225-1231, 1978.

The synthesis of analogues of the antipsychotic drug butaclamol bearing chloro substituents on the benzene rings is described. On the basis of a perceived topographical similarity of a putative chlorophenylethylamine pharmacophore present in these analogues and in VUFB-10032 and doclothepin (agents related to octoclothepin which do not induce catalepsy), they were tested with rats for noncataleptic neuroleptic activity. None of the butaclamol analogues exhibit this type of activity. Depending on the position of the chlorine, the analogues either retained butaclamol-like activity or were inactive. 37 references. (Author abstract)

002002 Iijima, Ikuo; Minamikawa, Jun-ichi; Jacobson, Arthur E.; Brossi, Arnold; Rice, Kenner C.; Klee, Werner A. Laboratory of Chemistry, National Institute of Arthritis, Metabolism and Digestive Diseases, Bethesda, MD 20014 **Studies in the ()-morphinan series. 5. Synthesis and biological properties of ()-naloxone.** Journal of Medicinal Chemistry. 21(4):398-400, 1978.

()-Naloxone was examined in three assay systems using guinea pig ileum and found to have no more than 1/1000-1/10,000th the activity of (-)-naloxone. ()-Naloxone was prepared in 26% overall yield in eight steps from ()-7-bromodihydrocodeinone dimethyl ketal by a synthesis which excluded enantiomeric contamination. It is concluded that ()-naloxone can serve to test the stereospecificity of the biochemical and pharmacological actions of (-)-naloxone. 13 references. (Author abstract modified)

002003 Kollonitsch, J.; Patchett, A. A.; Marburg, S.; Maycock, A. L.; Perkins, L. M.; Doldouras, G. A.; Duggan, D. E.; Aster, S. D. Merck Sharp & Dohme Research Laboratories, PO Box 2000, Rahway, NJ 07065 **Selective inhibitors of biosynthesis of aminergic neurotransmitters.** Nature (London). 274(5674):906-908, 1978.

In a study of inhibitors of biosynthesis of aminergic neurotransmitters, the transformation of amino acids into the corresponding substituted 3-fluoro-alanines, resulting in potent time dependent decarboxylase inactivators is reported. The preparation of the fluoromethyl derivatives corresponding to some of the amine products of these decarboxylases, and the determination of them as inactivators, are also reported. 29 references.

002004 Lemaire, Simon; Berube, Alain; Derome, Gilles; Lemair, Irma; Magnan, Jacques; Regoli, Domenico; St-Pierre, Serge. Dept. of Pharmacology, Centre Hospitalier Universitaire, Sherbrooke, Quebec J1H 5N4 Canada **Synthesis and biological activity of beta-endorphin and analogues: additional evidence for multiple opiate receptors.** Journal of Medicinal Chemistry. 21(12):1232-1235, 1978.

The solid phase synthesis of highly purified sheep beta-endorphin and three analogues is reported. Synthetic sheep beta-endorphin was found identical with the natural hormone by several analytical criteras as well as by three biological tests. Relative potencies of the synthetic compounds were estimated by their ability to inhibit the electrically evoked contractions of the guinea-pig ileum and of the rat vas deferens and to compete with tritiated naloxone for opiate receptors on rat brain homogenates. Introduction of D-Ala in position 2 of sheep beta-endorphin induces a 58% increase in its activity with the rat vas deferens and (3H)naloxone binding tests, whereas a dramatic decrease in the activity was found with the guinea-pig ileum bioassay. Further substitution of (D-Ala2, MePhe4) beta-endorphin, introducing Met (O) in position 5, does not induce any additional change in the biological activity of the parent peptide. The heterogeneity of responses caused by a specific modification in beta-endorphin strongly indicates the existence of more than one type of receptor for the opioid peptide. 33 references. (Author abstract modified)

002005 Lumma, William C., Jr.; Hartman, Richard D.; Saari, Walfred S.; Engelhardt, Edward L. Hirschmann, Ralph; Clin-

eschmidt, B. V.; Torchiana, M. L. Merck Sharp and Dohme Research Laboratories, West Point, PA 19486 **Piperazinylpyrazines with central serotoninmimetic activity.** Journal of Medicinal Chemistry. 21(6):536-542, 1978.

A series of 2-(1-piperazinyl)pyrazines was synthesized and evaluated for central serotoninmimetic activity. The most interesting member of the series, 6-chloro-2-(1-piperazinyl)pyrazine (3a), had pharmacological properties characteristic of potent central serotoninmimetic activity and only weak peripheral serotoninmimetic action. Structural similarities between 3a and serotonin are discussed. 36 references. (Author abstract)

002006 Markey, S. P.; Shaw, G. John. Laboratory of Clinical Science, NIMH, Bldg. 10, 2D-46, 9000 Rockville Pike, Bethesda, MD 20014 **Preparation of highly enriched diazomethane-2H2. (Unpublished paper).** Bethesda, MD, NIMH, 1978. 8 p.

Phase transfer catalyzed exchange of diethyl ether solutions of diazomethane (generated from nonlabeled nitrosamide precursors) with D20 and NaOD was determined to produce 99% labeled products as measured by reaction with benzoic acid-OD. Several solvent mixtures and phase transfer catalysts were used to promote rapid exchange with minimum decomposition. Equilibration was reached in 20 to 30 minutes with each of the four solvent systems tested, with the phase transfer catalysts promoting higher incorporation of deuterium more rapidly. The curves describing systems 1 and 2 plateau before reaching the theoretical enrichment if all the D20 were accessible for exchange and are best fit with a function reflecting separate rates for exchange and solubility. Multiple exchanges were effected by mixing fresh aqueous solutions in systems 1 to 4 in a microgenerator, separating the phases after 15 min, and either reacting the diazomethane with benzoic acid-OD or mixing with additional acqueous phase. An exchange time of 15 min was chosen as a compromise between enrichment and yield of diazomethane. Highest enrichments were observed in systems 1 and 4. 9 references. (Author abstract modified)

002007 Mendelson, Wallace B. Bldg. 10, National Institute of Health, Bethesda, MD 20014 **Pharmacologic and electrophysiologic effects of ethanol in relation to sleep. (Unpublished paper).** Bethesda, MD, NIMH, 1978. 34 p.

The interrelationships between the ingestion of ethanol and the metabolism of the neurotransmitters thought to play a major role in sleep regulation were investigated. Data suggesting that the biogenic amines and acetylcholine play an important role in the regulation of sleep are summarized, and the effects of ethanol on sleep are described. Multiple dose administration of ethanol in rats produces initial decreases in REM sleep, followed by a gradual return to baseline amounts, and a rebound increase when ethanol is discontinued. Two hypotheses relating sleep and alcoholism are suggested, based on the study of this REM rebound. While these hypotheses have heuristic value, they do not account for a variety of reported observations. Alterations in the metabolism of the biogenic amines and acetylcholine are one of many effects of ethanol. It is concluded, however, that the actions on the biogenic amines and acetylcholine are so complex that it is not possible to relate a specific metabolic effect to a particular change in sleep. 56 references.

002008 Neptune, Marilyn; McCreery, Richard L. Department of Chemistry, Ohio State University, Columbus, OH 43210 **Chemical and electrochemical oxidation of 7-hydroxychlorpromazine.** Journal of Medicinal Chemistry. 21(4):362-368, 1978.

The oxidation of 7-hydroxychlorpromazine, a process associated with several side-effects of chlorpromazine therapy, was examined in vitro by electrochemistry and rapid scanning spectrophotometry. At pH 2, the oxidation resulted in a quantitative yield of 7,8-dioxochlorpromazine, but several intermediates were observable during the course of the reaction. The concentrations of each intermediate were determined quantitatively as a function of time, and a complete oxidation mechanism is proposed. It is concluded that the interactions of the products of 7-hydroxychlorpromazine oxidation with their physiological environment may explain some of the side-effects of long-term chlorpromazine therapy. 32 references. (Author abstract modified)

002009 Stutz, Peter L.; Stadler, Paul A.; Vigouret, Jean-M.; Jaton, Annelise. Chemical Research, Pharmaceutical Department, Sandoz Ltd., Basel, Switzerland **Ergot alkaloids. New ergolines as selective dopaminergic stimulants.** Journal of Medicinal Chemistry. 21(8):754-757, 1978.

A new two step sequence for the epimerization of methyl dihydrolsergate at C-8 leading to methyl dihydroisolysergate is presented. The latter compound was used as starting material for the synthesis of various ergolines, of which (5R,8R,10R)-8-(cyanomethyl)-6-methylergoline (compound 4) is a very strong and long lasting central dopaminergic agent. Compound 4 and (5R,8R)-8-((2-pyridyl) thiomethyl)-6-methylergolene were tested for their ability to inhibit ovum implantation and to depress serum prolactin levels in rats. The results indicate that selective dopaminergic activity can be successfully achieved by chemical variation of ergot structures. 24 references. (Author abstract modified)

002010 Swahn, Carl-Gunnar; Beving, Hakan; Sedvall, Goran. Laboratory of Experimental Psychistry, Dept. of Psychiatry, Karolinska Hospital, S-104 01, Stockholm, Sweden **Synthesis of 4-amino-2,2,2,2 tetradeuterio 3-p chlorophenylbutyric acid (baclofen). (Unpublished paper).** Research Report, NIMH Grant 5R01-MH-27254, 1978. 10 p.

The synthesis of 4-amino-2,2,2,2-tetradeuterio-3-p-chlorophenylbutyric acid (baclofen) is described. The synthesis involves base catalyzed substitution of deuterium for hydrogen in 3-p-chlorophenylgutaric acid which is subsequently transformed to baclofen. The overal yield of baclofen by this synthesis was 80%. The baclofen contains only minor volatile impurities and can be used for the mass fragmentographic procedure for the determination of 4-amino-3-p-chlorophenylbutyric acid in body fluids. 4 references. (Author abstract modified)

002011 Walker, Richard B.; Ayres, James W.; Block, John H.; Lock, Albert. Department of Pharmaceutical Science, School of Pharmacy, Oregon State University, Corvallis, OR 97331 **tert-Butoxycarbonyl as a convenient protecting group in synthesis of potential centrally active dopamine derivatives.** Journal of Pharmaceutical Sciences. 67(4):558-559, 1978.

Several pivaloyl and pivaloyloxy esters and amides of dopamine (DA) were synthesized for possible antiparkinson activity. The compounds were synthesized by select O-acylation, N-acylation, and N-methylation procedures. The tert-butoxycarbonyl function was an effective and easily removed nitrogen protecting group for DA. Preliminary biological testing results showed that all compounds tested elicited a hypothermic response in mice, while only 0,0-dipivaloyl-N,N-dimethyldopamine reversed reserpine-induced motor depression in mice. However, these preliminary data are not sufficient to conclude that the observed biological effects were due to central DA receptor stimulation. 21 references. (Author abstract)

002012 Weder, H. G. Pharmazeutisches Institut, ETH-Honggerberg, CH-8093 Zurich, Switzerland **The interaction of central acting drugs with glutamate dehydrogenase.** Arzneimittel Forschung (Aulendorf). 28(5):752-755, 1978.

Evidence is presented that the neuroleptics chlorpromazine, fluphenazine, triflupromazine, and thioridazine affect the aggregation of glutamate dehydrogenase by binding to one single site of the polypeptide chain, possibly the GTP site. This interaction could be of biological importance for the degree of activity at high enzyme concentrations found in vivo. Amitriptyline and fluorazepam also bind to a specific single site of the polypeptide chain without affecting the aggregation of the oligomers. Because of the rather low affinity of these sites, the binding of the drugs in vivo does not cause a concentrating effect in the mitrochondria. 16 references. (Author abstract)

002013 Williams, Lyall R.; Lap, Bui V.; Lim, Chen H.; Temple, Diana M.; Easson, Peter A.; Letts, Gordon L. School of Chemistry, Macquarie University, North Ryde, 2113 New South Wales, Australia **2-Methoxyphenylethanolamines, potential beta-adrenergic blocking agents.** Journal of Medicinal Chemistry. 21(10):1081-1084, 1978.

The effect of the introduction of a 2-methyl substituent on the beta-adrenergic antagonistic properties of a series of 3-substituted and 4-substituted phenylethanolamines was studied. Both the series of bromo substituted and methyl substituted compounds behaved similarly, indicating that electronic forces are not significant in determining beta-adrenergic antagonist activity. When compared with the corresponding phenylethanolamines without a 2-methoxy substituent, the 2-methoxy-4 substituted derivatives had enhanced potency and selectivity, but the 2,3-distribution and 2,5-disubstitution patterns showed a loss of activity. The inconsistent changes in activity prevented any firm conclusions from being drawn about the effect of the ether oxygen and the beta-adrenoceptor antagonistic activity of phenoxypropanolamines. 20 references. (Author abstract)

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

002014 Bagolini, C; de Witt, P; Pacifici, L.; Ramacci, M. T. Research Laboratoreis Sigma-Tau, I-00040 Pomezia, Rome, Italy **Synthesis and pharmacological activity and some derivatives of 1 phenyl-1,2,3,4-tetrahydro- 5H-1,4 benzodiazepin-5-one.** Journal of Medicinal Chemistry. 21(5):476-480, 1978.

A series of 4-N-alkylamino derivatives and corresponding ammonium quaternary salts of tetrahydro-1,4-benzodiazepin-5-one was synthesized and evaluated for psychotropic activity in mice. Some nitro and amino derivatives of tetrahydro-1,4-benzodiazepin-5-one were also studied. The compounds were devoid of tranquilizing activity. Compared with the classical benzodiazepines chlordiazepoxide and diazepam, these compounds were highly toxic and had little or no effect on motor coordination, motor activity, and maximal electroshock. However, the compounds exhibited some pharmacological activity when used at high concentrations on some in vitro tests. 25 references. (Author abstract modified)

002015 Clarke, Frank H.; Hill, Ronald T.; Koo, John; Lopano, Rose M.; Maseda, Miguel A.; Smith, Michael; Soled, Steven; VonVeh, Gisbert. Research Department, Pharmaceuticals Division, CIBA-GEIGY Corporation, Ardsley, NY 10502 **A series of hexahydro(1,4)oxazino(3,4-a)isoquinolines as potential neuroleptics.** Journal of Medicinal Chemistry. 21(8):785-791, 1978.

A series of hexahydro(1,4)oxazino(3,4-a)isoquinolines were examined as potential neuroleptics in gerbils. The synthesis and stereochemistry of trans-N,N-diethyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro(1,4) oxazino(3,4-a)isoquinoline-3-carboxamide hydrochloride (compound 16) and a series of analogues are described. Compound 16 and its () isomer had neuroleptic properties in the Sidman avoidance test in gerbils. A few closely related amides of the trans series were active but cis amides were inactive as neuroleptics. It is concluded that although compound 16 is not a very potent neuroleptic, of the compounds examined, it is the one that most closely resembles benzquinamide and tetrabenazine in chemical structure. 13 references. (Author abstract modified)

002016 Conde, S.; Madronero, R. , Department of Chemistry, Instituto de Quimica Medica, Juan de la Cierva-3,Madrid-6, Spain **Effects of thiophene analogues of chloroamphetamines on central serotonergic mechanisms.** Journal of Medicinal Chemistry. 21(9):978-981, 1978.

Ring-chlorinate thienylisopropylamines (thiophene analogues of chloroamphetamines) were synthesized and evaluated for central serotonergic effects in male Wistar rats. A pharmacological profile similar to that of p-chloroamphetamine was found for 4,5-dichlorothienylisopropylamine; the compound produced long-lasting serotonin depletion and prolonged inhibition of synaptosomal uptake of serotonin. Chloro substitution in position C3 of the thiphene ring did not determined brain serotonin depletion or serotonin uptake inhibition but enhanced the brain monoamine oxidase inhibitory activitiy of the compounds. The inhibition of serotonin uptake was more marked that serotonin depletion only after 3,5-dichlorothienylisopropylamine. 34 references. (Author abstract modified)

002017 Corral, Carlos; Lissavetzky, Jaime; Madronero, Ramon. Instituto de Quimica Medica, Juan de la Cierva, 3, Madrid 6, Spain **Analogues of antipsychotic phenothiazines 10-(2-N',N'-disubstituted hydrazinoethyl) phenothiazines.** European Journal of Medicinal Chemistry (Paris). 13(4):389-391, 1978.

The synthesis of a series of selected 10-(2-N',N'-disubstituted hydrazinoethyl) phenothiazines is described. The compounds are isosteres of the known antipsychotic agents promazine, chlorpromazine, and prochlorperazine. Although these compounds produced behavioral depression in mice, no evidence of neuroleptic activity was observed. 7 references. (Author abstract modified)

002018 Ellefson, Charles R.; Woo, Chi M.; Miller, Arni; Kehr, Janet R. Searle Laboratories, Chicago, IL 60680 **Synthesis and biological evaluation of some 2-amino-4-aryl-3H-1,5-benzodiazepine analogues of clozapine.** Journal of Medicinal Chemistry. 21(9):952-957, 1978.

A series of 2-amino-4-aryl-3H-1,5-benzodiazepine analogues of clozapine was prepared and evaluated for potential neuroleptic activity. One compound showed some activity in blocking d-amphetamine-induced lethality, decreasing conditioned avoidance responses, increasing brain dopamine turnover, and inhibiting dopamine sensitive adenylate cyclase activity, but these effects were not consistently observed in other members of the series. Results indicate that structural modifications of clozapine lead to a decrease in activity. It is concluded that the 1,5-benzodiazepine portion of clozapine is not responsible for the drug's antipsychotic activity. 18 references. (Author abstract modified)

002019 Frincke, James M.; Henderson, Gary L.; Janssen, Paul A. J.; Van der Eycken, Cyriel A. M. Dept. of Pharmacology, University of California, Davis, CA 95616 **Synthesis and analgesic activity of some long-acting piperidinospiro derivatives of methadone.** Journal of Medicinal Chemistry. 21(5):474-476, 1978.

A congener of methadone, in which the metabolically labile C-6 dimethylamino moiety was replaced with a piperidinospiro derivative, was reduced and acetylated. This conversion produced a marked increase in the duration of analgesia in Sprague-Dawley rats, a trend similar to that found for methadone. However, conversion of the alcohol of the methadone series to the ester caused a large increase in potency in the methadone series

but not in the experimental series. 9 references. (Author abstract modified)

002020 Iorio, Maria A.; Casy, Alan F. Laboratory of Pharmaceutical Chemistry, Istituto Superiore di Sanita, I-00161 Rome, Italy **Nalorphine-like properties of some 2,3-dimethyl-3-arylpiperidines.** Journal of Medicinal Chemistry. 21(8):812-815, 1978.

A number of N-substituted 2,3-dimethyl-3-arylpiperidines having an m- or p-arylhydroxyl were prepared and evaluated for analgesic agonist and antagonist properties by the fentanyl antagonism test in rats. The diastereomeric N-allyl and N-cyclopropylmethyl derivatives behaved as pure potent antagonists. Substitution of the arylhydroxyl from the meta to the para position resulted in a net fall of the antagonist activity. The results demonstrate that potent antagonists can be found in relatively simple molecules such as 3-arylpiperidines providing that they possess an aryl hydroxyl in the meta position and a proper substituent on nitrogen. 20 references. (Author abstract modified)

002021 Kamioka, T.; Nakayama, I.; Hara, T.; Takagi, H. Central Research Laboratories, Sankyo Co., Ltd., 2-58, 1-chome Hiromachi, Shinagawa-ku, Tokyo, Japan **Pharmacological studies on CS-430, a new psychotropic agent.** Arzneimittel Forschung (Aulendorf). 28(5):838-847, 1978.

The properties of a new psychotropic agent, 10-bromo-11b-(2-fluorophenyl)-2,3,7,11b-tetrahydrooxazolo (3,2-d)(1,4)benzodiazepin-6(5H)-one (CS-430), are reported. The compound showed sleep inducing effects at both 0.2and 5mg/kg (p.o.)in cynomolgus monkeys or at 3mg/kg (p.o.)in rats. CS-430 showed selective conflict attenuating behavior in rats or anticonvulsant effects in mice. It blocked the nondiscriminated (Sidman) avoidance response without severe impairment of motor function, but did not block discriminated (shuttlebox) avoidance in rats. Selectively electroshock-induced fighting behavior of mice was also blocked, but not isolation-induced fighting in mice or muricidal behavior induced by ablation of the olfactory bulbs. CS-430 produced specific potentiation of chlorprothixene-induced sleep and particular potentiation of thiopental in mice. These effects are similar to those of nitrazepam, but not phenobarbital. The potency effect on motor function was roughly half that of nitrazepam. 62 references. (Author abstract modified)

002022 Kukla, Michael J.; Woo, Chi M.; Kehr, Janet R.; Miller, Arni. Dept. of Chemistry, G. D. Searle and Company, Chicago, IL 60680 **5-Chloro-2-phenyl-1-benzo(b)thiophene-3-alkanamines, potential antipsychotic agents.** Journal of Medicinal Chemistry. 21(4):348-352, 1978.

The 5-chloro-2-phenyl-1-benzo(b)thiophene-3-alkanamines were synthesized on the basis of the N-methylation hypothesis of schizophrenia and were evaluated in dopamine and haloperidol receptor assays with calf brain preparations. The binding characteristics were comparable in some cases to known neuroleptics. It is concluded that of primary concern is the possible involvement of this neurotransmitter (N-methylation) in the etiology of the disease state and the apparent similarity of all antipsychotic agents in the blockade of dopamine functions. 15 references. (Author abstract modified)

002023 Leonard, B. E. Pharmacology Department, University College, Galway, Ireland **Mianserin, an antidepressant with a unique neuropharmacological profile.** Acta Psychiatrica Belgica (Brussels). 78(5):770-780, 1978.

Research with mianserin, an antidepressant with a unique neuropharmacological profile, is reviewed, emphasizing that it has a behavioral profile which more closely resembles that of an anxiolytic than an antidepressant and that it does not reverse reserpine-induced hypothermia in mice. This suggests that it does not reduce the reuptake of biogenic amines into the neuron from the synaptic cleft as do imipramine type drugs. Data were obtained on the effect of mianserin on dopamine, noradrenaline, and 5-hydroxytryptamine as compared with tricyclic antidepressants of the imipramine type. The findings indicate that mianserin is an antidepressant with a unique mode of action on brain monoamine metabolism. Drugs such as mianserin and iprindol challenge the popular assumption that a compound must inhibit the amine reuptake mechanisms before it can be considered as a potential antidepressant. 15 references. (Journal abstract modified)

002024 Lindberg, Ulf Henrik; Thorberg, Seth-Olof; Bengtsson, Stefan; Renyi, Anna L.; Ross, Svante B.; Ogren, Sven-Ove. Dept. of Organic Chemistry, CNS Drugs, Astra Lakemedel AB, S-151 85 Sodertalje, Sweden **Inhibitors of neuronal monoamine uptake. 2. Selective inhibition of 5-hydroxytryptamine uptake by alpha-amino acid esters of phenethyl alcohols.** Journal of Medicinal Chemistry. 21(5):448-456, 1978.

In a study of potential antidepressant drugs, a series of alpha-amino acid esters of substituted phenethyl alcohols was prepared and evaluated for inhibition of neuronal reuptake of noradrenaline and 5-hydroxytryptamine (5HT) in male NMRI mice. Some of the compounds, particularly alaproclate, were potent and very selective inhibitors of 5-HT uptake. Data were analyzed in terms of structure/activity relationships, and a hypothetical carrier site for 5-HT uptake was deduced from geometry and electronic properties. 37 references. (Author abstract modified)

002025 Osbahr, Albert J., III; Nemeroff, Charles B.; Manberg, Paul J.; Prange, Arthur J., Jr. Biological Sciences Research Center, University of North Carolina, School of Medicine, Chapel Hill, NC 27514 **Centrally administered neurotensin: activity in the Julou-Courvoisier muscle relaxation test in mice.** European Journal of Pharmacology (Amsterdam). 54(3):299-302, 1979.

Intracisternal administration of neurotensin (NT) to male Swiss-Webster produced muscle relaxation in the Julou-Courvoisier traction test, a screening procedure used to assess neuroleptic drug activity, but no dose/response relationship was observed. Intracisternal administration of thyrotropin releasing hormone totally abolished the effects of NT. Two other peptides, substance P and bradykinin, were inactive in the traction test. Results indicate that NT exerts neuroleptic-like activity in a screening test for antipsychotic agents. 10 references. (Author abstract modified)

002026 Portoghese, P. S.; Larson, D. L.; Jiang, J. B.; Takemori, A. E.; Caruso, T. P. Department of Medicinal Chemistry, College of Pharmacy, University of Minnesota, Minneapolis, MN 55455 **6Beta (N,N-bis(2-chlorethyl)amino) 17-cyclopropylmethyl) 4,5alpha epoxy-3,14-dihydroxymorphinan (chlornaltrexamine), a potent opioid receptor alkylating agent with ultralong narcotic antagonist activity.** Journal of Medicinal Chemistry. 21(7):598-599, 1978.

The synthesis and narcotic antagonist activity of 6beta-(N,N-bis(2-chloroethyl)amino)-17-(cyclopropylmethyl) 4,5alpha-epoxy-3,14-dihydroxymorphinan or chlornaltrexamine (CNA) is described. CNA showed no analgesic effect of its own at intracerebroventricular (i.c.v.)doses of 0.6, 1.2, 2.4, or 4.8nmol/mouse. However, i.c.v. or i.p. injected CNA exhibited significant dose dependent inhibition of morphine analgesia; this antagonistic effect was apparent as long as 3 days after injection, but was not detected after 6 days. Naloxone pretreatment blocked the effect of i.c.v. CNA on morphine analgesia. CNA

also inhibited in vitro binding of tritiated naloxone to opioid receptors. Results suggest that CNA produces long-lasting narcotic antagonism through co alent association with the same receptors that reversibly blind naloxone and naltrexone. 23 references.

002027 Rasmussen, C. R.; Gardocki, J. F.; Plampin, J. N.; Twardzik, B.; Reynolds, B.; Molinari, A.; Schwartz, N.; Bennetts, W.; Price, B.; Marakowski, J. Department of Chemical Research, McNeil Laboratories, Fort Washington, PA 19034 **2-Pyrrolidinylideneureas, a new class of central nervous system agents.** Journal of Medicinal Chemistry. 21(10):1044-1054, 1978.

A series of N-aryl-N'-(1-methyl-2-pyrrolidinylidene)ureas, a new class of central nervous system (CNS) agents, was prepared and screened for pharmacologic activity. Congeners possessing either phenyl or phenyl substituted with 4-nitro, 3-bromo, 3-chloro, 3-fluoro, and 3-methyl groups were found to demonstrate anxiolytic activity in rat. 2,6-Disubstitution of the phenyl ring with methyl, chloro, and bromo imparted potent muscle relaxant properties which appeared to be centrally mediated. A significant separation of the anxiolytic and muscle relaxant properties from other CNS activities (eg. anticonvulsant, sedative, and hypnotic) was achieved. 32 references. (Author abstract modified)

002028 van Riezen, H.; van der Burg, W. J. Organon Scientific Development Group, Organon International, B.V. Oss 5340 BH, The Netherlands **The pharmacology of mianserin (Org. GB 94) Leviron, a really different antidepressant.** Acta Psychiatrica Belgica (Brussels). 78(5):756-769, 1978.

The pharmacological properties of the new tetracyclic antidepressant, mianserin, were studied, demonstrating that it clinically outperforms a placebo and has less side effects than the tricyclic antidepressants. Structurally, it has neither anticholinergic activity nor is it effective in classical tests of antidepressant activity based on amine reuptake inhibition. Mianserin shows clear antidepressant activity in tests with muricide rats, in bulbectomized rats, and in the acquired immobility test with rats or mice. It has effects indicative of anxiolytic activity in several tests, including those using punishment or conflict paradigms. Mianserin is less toxic in the cardiovascular system than the tricyclic antidepressants. In chronic administration to rats and mice, it does not produce dependence or abstinence. 64 references. (Journal abstract modified)

002029 Voith, Katherine; Bruderlein, Francois T.; Humber, Leslie G. Department of Pharmacology, Ayerst Research Laboratories, Montreal, Quebec, Canada **Neuroleptics related to butaclamol. Synthesis and some psychopharmacological effects of a series of 3-aryl analogues.** Journal of Medicinal Chemistry. 21(7):694-698, 1978.

The synthesis and pharmacological effects of 16 3-aryl analogues of butaclamol, a new antipsychotic drug are described. The compounds were evaluated for their abiltiy to antagonize d-amphetamine-induced stereotyped behavior, disrupt conditioned avoidance behavior, protect against epinephrine-induced mortality, and induce catalepsy. Results indicate that the 3-substituent plays a critical role with regard to neuroleptic potency and tendency to induce extrapyramidal side-effects and hypotension. 26 references. (Author abstract modified)

002030 Wikstrom, Hakan; Lindberg, Per; Martinson, Per; Hjorth, Stephan; Carlsson, Arvid; Hacksell, Uli; Svensson, Uno; Nilsson, J. Lars G. Department of Pharmacology, University of Goteborg, Fack, S-400 33 Goteborg, Sweden **Pivaloyl esters of N,N-dialkylated dopamine congeners. Central dopamine-receptor stimulating activity.** Journal of Medicinal Chemistry. 21(9):864-867, 1978.

A series of compounds was tested for dopamine receptor stimulating activity, using a new biochemical screening method in conjunction with behavioral testing in reserpinized rats. Of a series of dipivaloyl-N,N-dialkyldopamines studied, O',O'-dipivaloyl-N,N-dipropyldopamine was the only active derivative. However, the monopivaloyl ester 2-(3-pivaloyloxyphenyl)-N,N-N-dipropylethylamine was more potent. The same relationship was found for the corresponding phenols, N,N-dipropydopamine and 2-(3-hydroxyphenol)-N,N-dipropylethylamine, but both were more active than their pivaloyl esters. 33 references. (Author abstract modified)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

002031 Ahn, Ho Sam; Feldman, Susan C.; Makman, Maynard H. Schering Corporation, Bloomfield, NJ 07003 **Posterior pituitary adenylate cyclase: stimulation by dopamine and other agents.** Brain Research (Amsterdam). 166(2):422-425, 1979.

Dopamine (DA) stimulated the adenylate cyclase activity in homogenates of posterior pituitary from male Sprague-Dawley rats in a dose dependent fashion, with maximal stimulation occurring at 50-100mcM DA. The DA receptor agonist, apomorphine, also significantly stimulated enzyme activity in the posterior pituitary. The DA stimulated activity was more effectively blocked by haloperidol (a relatively specific DA receptor blocker) than by phentolamine (an alpha-adrenergic receptor blocker) or propranolol (a beta-adrenergic receptor blocker). Posterior pituitary adenylate cyclase was also stimulated by norepinephrine, isoproterenol, prostaglandin El, and the guanosine triphosphate analogue Gpp(NH)p. Adenylate cylase of 21 day fetal rat posterior pituitaries was significantly stimulated by catecholamines, but the response was much lower in fetal rats than in 2 month old rats. Results indicate the DA receptors and other receptor systems not yet characterized are coupled to adenylate cyclase in rat posterior pituitary. 20 references.

002032 Ahn, Ho Sam; Makman, Maynard H. Department of Biochemistry, Albert Einstein College of Medicine, Bronx, NY 10461 **Interaction of LSD and other hallucinogens with dopamine-sensitive adenylate cyclase in primate brain: regional differences.** Brain Research (Amsterdam). 162(1):77-88, 1979.

The effects of D-lysergic acid (LSD) and mescaline on adenylate cyclase (AC) activity were studied in homogenates of Cebus and rhesus monkey anterior limbic cortex (ALC), frontal cortex (FC), caudate nucleus, retina, and auditory cortex. LSD and mescaline stimulated AC activity in ALC and auditory cortex, but not in FC, caudate nucleus, and retina. LSD was able to antagonize dopamine stimulated AC activity in all brain regions examined. Although much weaker than LSD, methamphetamine also produced dose dependent stimulation of AC activity in ALC. Both agonist and antagonist effects of the hallucinogens appeared to involve interaction with dopamine receptors; LSD or methamphetamine stimulated AC activity in ALC was blocked by haloperidol and fluphenazine, but not by phentolamine. Antagonism of dopamine by LSD in ALC and FC was competitive, mescaline was an effective but weaker antagonist than LSD. The occurrence of dopamine agonistic action of hallucinogens in only certain regions of primate brain is discussed in relation to the behavioral effects of LSD, mescaline, and methamphetamine in primates. 45 references. (Author abstract modified)

002033 Al-Jeboory, Ali Awad; Marshall, Richard J. Dept. of Physiology and Pharmacology, University of Strathclyde, Glasgow G1 1XW, Scotland **Correlation between the effects of salbutamol on contractions and cyclic AMP content of isolated fast -- and slow -- contracting muscles of the guinea pig.** Naunyn-

Schmiedeberg's Archives of Pharmacology (Berlin). 305(3):201-206, 1978.

The effects of isoprenaline and salbutamol on incomplete tetanic contractions of the isolated soleus (slow contracting) and extensor digitorum longus (EDL, fast contracting) muscles of the guinea pig were studied and an attempt made to correlate these effects on contractility with changes in cyclic AMP (c-AMP) concentrations. Salbutamol was 10 to 12 times less potent than isoprenaline in decreasing the force of subtetanic contractions in the soleus and between five and six times less potent in increasing the force of subtetanic contractions in the EDL. This observation plus the lack of activity of both the selective beta1 adrenoceptor antagonist and the selective beta1 agonist in the EDL implies involvement of beta2 adrenoceptors in these responses of the muscles to isoprenaline and salbutamol. In concentrations which produced effects on muscle contractility, salbutamol significantly elevated c-AMP concentrations in both types of muscle. These effects were antagonized by propranolol. The contrasting effects of sympathomimetic amines on slow and fast contracting muscle are mediated through a common mechanism -- elevation of c-AMP. 27 references. (Author abstract modified)

002034 Aleksandrov, A. A. Kafedra vysshey nervnoy deyatel'nosti Leningradskogo gosudarstvennogo universiteta imeni A. A. Zhdanova, Leningrad, USSR **/Microiontophoretic study of the effect of GABA and taurine on the activity of the neurons of the feline motor cortex./** Mikroionoforeticheskoye issledovaniye deystviya GAMK i taurina na aktivnost' neyronov motornoy kory koshki. Fiziologicheskiy Zhurnal SSSR imeni I. M. Sechenova (Leningrad). 64(8):1057-1065, 1978.

An experiment was conducted to determine the effect of GABA and taurine on the motor cortex of cats. Nembutal anesthesis was administered to a number of laboratory animals in a dosage of 35 to 40mg/kg, and their extremities and pyramidal tracts were stimulated with electrodes. The effect of GABA on neuronal activity under these conditions was studied in connection with 65 neurons of the rear sinuosity of the cortex, while the effect of taurine was recorded for 41 neurons. Six charts illustrate these effects on the background activity of the neurons. High sensitivity to GABA was revealed. Certain neurons also registered a high sensitivity to taurine. The effects of taurine on the spontaneous and evoked unit activity suggest that this amino acid is a synaptic transmitter in the cerebral cortex. 19 references. (Journal abstract modified)

002035 Anden, Nils-Erik; Grabowska-Anden, Maria; Wachtel, Helmut. Dept. of Pharmacology, University of Goteborg, S-400 33 Goteborg, Sweden **Effects of the GABA receptor agonist muscimol on the turnover of brain dopamine and on the motor activity of rats.** Acta Pharmacologica et Toxicologica (Kobenhavn). 44(3):191-196, 1979.

Muscimol (10mg/kg ip) elevatd the concentration of dopamine, decreased the utilization of dopamine, and increased the synthesis of dopamine in male Sprague-Dawley rat brain. Muscimol also accelerated the utilization of noradrenaline. Local application of muscimol to the nucleus accumbens inhibited motor activity in a dose dependent manner, with only a slight subsequent hyperactivity. These effects are similar to those produced by gamma-aminobutyric acid (GABA) and support the view that muscimol is a GABA receptor agonist. 33 references. (Author abstract modified)

002036 Andrews, C. D.; Davis, A.; Freeman, H. S; McDermed, J. D.; Poat, Judith A.; Woodruff, G. N. Department of Physiology & Pharmacology, University of Southampton, Southampton, England **Effects of ()- and (-)-enantiomers of 2 amino-6,7-dihydroxy 1,2,3,4 tetrahydronaphthalene on dopamine receptors and on dopamine uptake.** British Journal of Pharmacology (London). 64(3):433P, 1978.

In a paper presented at the September 1978 meeting of the British Pharmacological Society at the University of Nottingham, the effects of the ()-enantiomers and (-)-enantiomers of 2-amino-6,7-dihydroxy-1,2,3,4-tetrahydronaphthalene (ADTN) on dopamine (DA) receptors and DA uptake in rats are reported. The effects of ()-hydrobromide and (-)-ADTN hydrobromide on rat striatal DA sensitive adenylate cyclase and on locomotor activity following bilateral injections into the nucleus accumbens were assessed. On the striatal DA sensitive adenylate cyclase assay, ()-ADTN was approximately 100 times more active than (-)-ADTN in increasing cyclic adenosine monophosphate production. The ()-enantiomer was approximately 13 times more active than (-)-ADTN in stimulating locomotor activity. In synaptosomes prepared from rat striatum, ()ADTN was more active than (-)-ADTN in inhibiting uptake of (3H)DA. 2 references. (Author abstract modified)

002037 Argiolas, A.; Fadda, F.; Stefanini, E.; Gessa, G. L. Institute of Pharmacology and Physiology, University of Cagliari, Via Porcell 4, I-09100 Cagliari, Italy. **Evidence for a direct action of amphetamine on dopamine metabolism in the rat substantia nigra in vivo.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 301(3):171-174, 1978.

Evidence for a direct action of amphetamine on dopamine metabolism in the rat substantial nigra in vivo is presented. The intraperitoneal administration of D-amphetamine (0.2-2.5mg/kg) decreases dihydroxyphenylacetic acid content not only in the caudate nucleus but also in the substantia nigra. This effect persists both in the substantia nigra and in the caudate nucleus after loss of dopamine sensitive adenylate cyclase and presumably of dopamine receptors induced by intrastriatal injection of kainic acid. These results indicate that the effect of amphetamine on dihidroxyphenylacetic acid levels in the nigra is not mediated through a strionigral feedback loop. 29 references. (Author abstract modified)

002038 Arqueros, Luis; Naquira, Daisy; Zunino, Edith. Dept. of Neurobiology, Institute of Biological Sciences, Catholic University, Santiago, Chile **Nicotine-induced release of catecholamines from rat hippocampus and striatum.** Biochemical Pharmacology (Oxford). 27(23):2667-2674, 1978.

A comparative study of (3H)catecholamine release from noradrenergic and dopaminergic neuron terminals of the CNS of rats induced by nicotine and potassium depolarization is reported. Striatal and hippocampal slices of rat brain that had incorporated (3H)catecholamines in previous incubations with the radioamines were superfused and stimulated by nicotine and high potassium. Nicotine produced a marked release from these two brain areas. Nicotine-induced release was dose dependent, inhibited by low temperature, independent of extracellular calcium, and not inhibited by an excess of magnesium. The release was continuous during prolonged nicotine stimulation in contrast to the transient efflux induced by prolonged stimulation by potassium, and additive when the slices were superfused simultaneously with nicotine plus potassium. It is concluded that this may explain in part some of the already known central effects of nicotine and its pharmacological similarities to amphetamine central effects. 23 references. (Author abstract modified)

002039 Austin, L.; Recasens, M.; Mandel, P. Centre de Neurochimie du CNRS, Institut de Chimie Biologique, 11, rue Humann, F-67085 Strasbourg Cedex, France **GABA in the olfactory bulb and olfactory nucleus of the rat: the distribution of gamma-aminobutyric acid, glutamic acid decarboxylase, GABA**

transaminase and succinate semialdehyde dehydrogenase. Journal of Neurochemistry (Oxford). 32(5):1473-1477, 1979.

The distribution of gamma-aminobutyric acid (GABA) and enzymes involved in its metabolism was investigated in different regions of the male Wistar rat olfactory bulb and and olfactory nucleus. The highest levels of GABA in the olfactory bulb were found in the layers rich in nerve terminals (31mcmol/g dry weight). A similar distribution was found in the olfactory nucleus, but the overall level of GABA was only about 25% of that in the bulb. Glutamic acid decarboxylase (GAD) activity in the various layers of the olfactory nucleus was similar in distribution to that of GABA, but the correlation of between GABA and GAD did not hold for the olfactory bulb. The activities of GAD and levels of GABA were significantly higher in the bulb than in the nucleus, but succinic acid semialdehyde dehydrogenase and GABA aminotransferase activities were almost identical in both regions. 16 references. (Author abstract modified)

002040 Awazi, N.; Guldberg, H. C. Dept. of Pharmacology, University of Trondheim, Regional Hospital, N-7000 Trondheim, Norway **On the formation of 6-hydroxyindoles in rat brain.** Journal of Pharmacy and Pharmacology (London). 30(12):793-795, 1978.

The metabolic fate of tryptamine was studied in Wistar rat brain, with particular reference to oxidative hydroxylation as a metabolic pathway for cerebral tryptamine. Both 6-hydroxytryptamine and 6-hydroxy-N-methyltryptamine were formed from tryptamine in rat brain homogenates. In addition, 6-hydroxyindoleacetic acid and 3-indoleacetic acid were formed both in vivo and in vitro. Results suggest that oxidative deamination may be a main pathway for the metabolism of tryptamine in vivo and in vitro. 11 references.

002041 Babitch, Joseph A.; Gage, Fred H.; Valdes, James J. Chemistry of Behavior Program, Texas Christian University, Fort Worth, TX 76129 **Effects of phalloidin on K-dependent, Ca2-independent neurotransmitter efflux and K-facilitated, Ca2-dependent neurotransmitter release.** Life Sciences (Oxford). 24(2):117-124, 1979.

The actions of phalloidin, a bicyclic heptapeptide that binds to actin, were investigated in rat brain synaptosomes preloaded with radioactive neurotransmitters and then depolarized to cause transmitter release. Phalloidin stimulated the potassium dependent, calcium independent efflux of gamma-aminobutyric acid and norepinephrine from synaptosomes, but inhibited the potassium facilitated, calcium dependent release of these neurotransmitters. These findings suggest that an actomyosin system is involved in synaptic transmission. 31 references. (Author abstract modified)

002042 Bakhanashvili, T. A.; Maysov, N. I.; Aleksidze, N. G.; Rayevskiy, K. S. Laboratoriya neyrokhimicheskoy farmakologii Instituta farmakologii AMN SSSR, Moscow, USSR **/Uptake of tryptophan by neuroglia cells and synaptosomes of the rabbit brain./** Zakhvat triptofana kletkami glii i sinaptosomami kory golovnogo mozga krolika. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 85(2):172-174, 1978.

An experiment was conducted in order to observe the process of tryptophan uptake by the neuroglia cells and synaptosomes of the rabbit brain. The cerebral cortex of a rabbit was removed and placed in an incubating medium, into which two types of L-tryptophan were introduced. The system of uptake by the neuroglia cells was characterized by a high affinity to tryptophan, while the synaptosomes were found to have a lower affinity. The psychotropic substances chlorpromazine and imipramine produced an inhibitory influence on neuroglia cell uptake. The leading role of the neuroglia cells in the trophic provision of the neurons and in the normal course of neurodynamic processes was confirmed. 14 references. (Journal abstract modified)

002043 Bala, R. M.; Bohnet, H. G.; Carter, J. N.; Friesen, H. G. Faculty of Medicine, Health Science Centre, University of Calgary, Calgary, Alberta, Canada T2N 1N4 **Effect of ovine prolactin on serum somatomedin bioactivity in hypophysectomized female rats.** Canadian Journal of Physiology and Pharmacology (Ottawa). 56(6):984-987, 1978.

Ovine prolactin (PRL) increased serum somatomedin (SM) bioactivity in hypophysectomized female Sprague-Dawley rats. This effect was augmented by small but not large doses of adrenocorticotrophic hormone. Results suggest that PRL may regulate SM production in the female rat. Adrenal factors may modulate SM production or serum SM bioactivity. 21 references. (Author abstract modifies)

002044 Barker, L. A.; Mittag, T. W.; Krespan, B. Department of Pharmacology, Mount Sinai School of Medicine, CUNY, New York, NY 10029 **Studies on substrates, inhibitors and modifiers on the high affinity choline transport-acetylation system present in rat brain synaptosomes.** In: Jenden, D., Cholinergic mechanisms and psychopharmacology. New York, Plenum, 1978. 885 p. Vol. 24. (p. 465-480).

At the third Symposium on Cholinergic Mechanisms and Psychopharmacology, held in La Jolla, CA, March 1977, a paper reviewing the high affinity transport of choline (Ch) in the synthesis of acetylcholine (ACh) by intact synaptosomes was presented. The effects of some known inhibitors of choline acetyltransferase (CAT) on the high affinity transport and acetylation of Ch; the transport and acetylation of some Ch analogs; the effect of N,N,N1,N-tetrakis(2-chlorethyl)-1,6-hexanediamine, an irreversible and relatively selective inhibitor of the high affinity carrier, on the transport of Ch and on the synthesis and release of ACh by K depolarized synaptosomes; and the transport of Ch by synaptosomes in the presence of an inhibitor of pyruvate dehydrogenase complex were studied. Results provide direct experimental support for the hypothesis that the synaptosomal high affinity transport of Ch is a reaction coupled process leading to the synthesis of ACh. Further, these findings show that the substrate specificity of solubilized CAT is not that of the enzyme in situ; but that the high affinity transport of Ch is one of the rate limiting steps in the synthesis of ACh, and that under conditions of depolarization, a functional high affinity carrier is required for the synaptosomal synthesis of ACh. 30 references.

002045 Barlow, S. M.; Knight, A. F.; Sullivan, F. M. Dept. of Pharmacology, Guy's Hospital Medical School, London SE1 9RT, England **Plasma corticosterone responses to stress following chronic oral administration of diazepam in the rat.** Journal of Pharmacy and Pharmacology (London). 31(1):23-26, 1979.

The effect of daily oral administration of diazepam on plasma corticosterone responses to stressors of varying intensity was investigated. In female Porton Wistar rats exposed to a mild stress (noise), 10mg/kg, but not 1.0or 0.1mg/kg, diazepam reduced plasma corticosterone concentrations by 30% compared to controls. However, in rats exposed to more severe stressors (footshock or immobilization), none of these doses of diazepam reduced plasma corticosterone responses. In unstressed rats, 10mg/kg diazepam raised plasma corticosterone concentrations. These results suggest that plasma corticosterone concentration is not a reliable indicator of the tranquilizing effect of diazepam during stress. 23 references. (Author abstract modified)

002046 Beaumont, Kevin; Maurin, Yves; Reisine, Terry D.; Fields, Jeremy Z.; Spokes, Ernest; Bird, Edward D.; Yamamura, Henry I. Dept. of Neuropharmacology, Synthelabo-LERS, Bagneux, France **Huntington's disease and its animal**

model: alterations in kainic acid binding. Life Sciences (Oxford). 24(9):809-816, 1979.

The density of kainic acid (KA) binding in control and Huntington's diseased (HD) human brain and the alterations of KA binding produced by striatal KA lesions in male Sprague-Dawley rats were examined. Tritiated KA binding was reduced by 55% in the caudate nucleus and by 53% in the putamen of HD brains, compared to controls. In rats given KA striatal lesions, 3H-KA binding underwent a slow reduction, reaching 25% of control after 6 weeks. Properties of 3H-KA binding to rat membranes (including inhibition by ions, regional distribution, and displacement by various compounds) indicate that the KA lesioned rat is a valid model for HD and suggest a postsynaptic location for KA receptors in the striatum. 20 references. (Author abstract modified)

002047 Ben-Barak, Jacob; Dudai, Yadin. Department of Neurobiology, Weizmann Institute of Science, Rehovot, Israel **Cholinergic binding sites in rat hippocampal formation: properties and ontogenesis.** Brain Research (Amsterdam). 166(2):245-257, 1979.

Studies of the specific binding of tritiated quinuclidinyl benzilate (3H-QNB) and of (125I) labeled alpha-bungarotoxin (aBtx) in the Wistar rat hippocampal formation revealed the presence of two types of membrane bound cholinergic binding sites, which differ in pharamacological profile, sensitivity to detergents, and ontogenesis. The major binding site (about 17pmol/adult hippocampus) bound 3H-QNE with an apparent dissociation constant (Kd) of 0.4nM; this binding was displaced by low concentrations of muscarinic ligands but not of nicotinic ligands. The earliest increase in binding level was detected at about 4 days after birth, and a sharp increase in binding level was observed between postnatal days 10 through 15. Total binding continued to increase gradually about three-fold until about 7 weeks of age, at a rate resembling that of acetylcholinesterase. In contrast, the aBtx binding sites (about 0.6pmol/adult hippocampus) displaed a nicotinic profile, with an apparent Kd of 2nM. Absolute aBtx binding reached mature levels at 12 to 14 days after birth, and binding per tissue protein was higher during the first postnatal days than at maturity. 37 references. (Author abstract modified)

002048 Bensemana, D.; Gascon, A. L. Departement de pharmacologie, Faculte de medecine, Universite de Montreal, Montreal, Quebec, Canada **Relationship between analgesia and turnover of brain biogenic amines.** Canadian Journal of Physiology and Pharmacology (Ottawa). 56(5):721-730, 1978.

The analgesic activity of morphine, delta9THC, and sodium salicylate was studied concomitantly with changes in brainstem and cortex turnover of dopamine (DA), noradrenaline (NA), and serotonin (5-HT). Results show that a correlation exists between the presence of analgesia and the increased turnover rates of the three biogenic amines. Morphine and sodium salicylate induced analgesia was accompanied by an increased turnover rate of all three biogenic amines; delta9THC-induced analgesia was accompanied by an increased turnover rate of DA and 5-HT only. There was, however, no consistent relationship between the degree of analgesia and the degree of change in the turnover rates. The existence of the endogenous morphine-like substances, endorphines, may explain why morphine analgesia is distinct from that of delta9THC and sodium salicylate. The possible relationship between this morphine-like substance and biogenic amines is discussed. 53 references. (Author abstract)

002049 Benzi, G.; Arrigoni, E.; Dagani, F.; Marzatico, F.; Manzini, A.; Pastoris, O.; Villa, R. F. Dept. of Science, Institute of Pharmacology, University of Pavia, Pavia, Italy **Drugs action on cerebral energy state during and after various hypoxic conditions.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 236(2):234-251, 1978.

The behavior of fuels (glycogen, glucose), of glycolytic pathway intermediates and end product (lactate), and of the pool of labile phosphates, and the energy charge of the brain were studied in the motor area of the cerebral cortex of beagle dogs. These parameters were assessed after various hypoxic conditions and after 3, 15, or 30 minutes of posthypoxic recovery and recirculation, and the effects of intracarotid perfusion of papaverine, UDP-glucose, (-)eburnamonine, and suloctidil were evaluated under each condition. None of the drugs proved able to improve the deranged brain metabolism under all the hypoxic conditions. On the contrary, an activating effect of suloctidil and (-)eburnamonine could be observed during the recovery after both hypoxia and hypoxia plus complete ischemia, papaverine being ineffective and UDP-glucose increasing the glycogen synthesis. None of the drugs were found to restore altered brain metabolism after hypoxia plus incomplete ischemia. 51 references. (Author abstract modified)

002050 Bittman, Eric L. Endocrinology Program, University of Michigan, Ann Arbor, MI 48109 **Hamster refractoriness: the role of insensitivity of pineal target tissues.** Science. 202(3468):648-650, 1978.

A series of experiments were undertaken to examine the role of pineal target tissues in the photoperiodicity of testicular refractoriness in the golden hamster. Hamsters whose gonads had spontaneously regressed in response to shorter photoperiods were injected with 25 micrograms melatonin once daily (known to induce regression in intact hamsters) or thrice daily (reported to arrest reproduction in pinealectomized hamsters) for 7 weeks. In neither case did refactoriness respond to melantonin treatment. The goands of intact hamsters treated with melatonin for 21 weeks regressed and spontaneously recrudesced along a normal time course. Results indicate that gonadal refractoriness is due to insensitivity of target tissues of the pineal gland and imply that melatonin participates in photoperiodic regulation of reproduction in the golden hamster. 22 references. (Author abstract modified)

002051 Block, Edward R.; Cannon, James K. Dept. of Medicine, University of Florida College of Medicine, Gainesville, FL 32610 **Effect of hyperoxia on imipramine uptake and metabolism by the isolated, perfused rat lung.** Research Communications in Chemical Pathology and Pharmacology. 22(3):621-624, 1978.

The effects of high partial pressures of oxygen on pulmonary uptake and metabolism of imipramine were investigated in isolated, perfused rat lung. Uptake of imipramine was calculated from the arteriovenous difference of 14C-imipramine across the lung and lung effluents and homogenates were analyzed for the presence of metabolites of imipramine. Imipramine was avidly concentrated in the lungs of control rats by a saturable process, and this saturable uptake was not affected by 12 to 48 hour exposure to 100% oxygen. 10 references. (Author abstract modified)

002052 Bohlen, Peter; Huot, Sylvie; Palfreyman, Michael G. Salk Institute, P.O. Box 1809, San Diego, CA 92112 **The relationship between GABA concentrations in brain and cerebrospinal fluid.** Brain Research (Amsterdam). 167(2):297-305, 1979.

Gamma-aminobutyric acid (GABA) concentrations in cerebrospinal fluid (CSF) and brain of male Sprague-Dawley rats and female cats were determined before and after administration of three drugs that increase brain GABA levels. In the CSF of untreated animals, very little free GABA and considerable amounts of conjugated GABA were observed. After i.p. injection of gamma-vinyl GABA to rats, CSF concentrations of both

free and conjugated GABA rose in a dose dependent manner. Rat whole brain GABA concentrations were exponentially correlated with free GABA in the CSF, whereas brain GABA was linearly correlated with conjugated GABA in the CSF. Gamma-acetylenic GABA had qualitatively similar effects to gamma-vinyl GABA. Treatment with ethanolamine-O-sulfate, in a dose that did not affect brain GABA concentration, markedly increased serum GABA level, significantly elevated free GABA in the CSF, and had no effect on conjugated GABA in CSF. Results suggest that total CSF GABA concentrations are related primarily to brain GABA levels and are minimally affected by changes in the peripheral GABA concentrations. Implications of these findings for the clinical use of drugs altering brain GABA levels in neurological and psychiatric disorders are discussed. 28 references. (Author abstract modified)

002053 Borg, J.; Balcar, V. J.; Mandel, P. Centre de Neurochimie du CNRS, 11 rue Humann, F-67085, Strasbourg Cedex, France **Effect of cyclic nucleotides on high affinity uptake of L-glutamate and taurine in glial and neuroblastoma cells.** Brain Research (Amsterdam). 166(1):113-120, 1979.

Cultured glial cells (clones NN and I6) and neuroblastoma cells (clones M1 and M1NN) were used to study the effect of cyclic nucleotides on the high affinity uptake of L-glutamate and taurine. Treatment of NN cells with a mixture of N6,2'-O-dibutyryl cyclic adenosine monophosphate and 8-bromocyclic guanosine monophosphate for 1 or 2 days more than tripled the maximum velocity of L-glutamate high affinity uptake. Similar but smaller changes were observed in the I6 glial clone. The cyclic nucleotide derivatives had slight or no effects on the high affinity uptake of L-glutamate by the neuroblastoma clones M1 and M1NN or of taurine by glial or neuroblastoma cells. 15 references. (Author abstract modified)

002054 Braestrup, Claus; Squires, Richard F. Psychopharmacological Research Laboratory, Sct. Hans Mental Hospital, DK-4000 Roskilde, Denmark **Brain specific benzodiazepine receptors.** British Journal of Psychiatry (London). 133(September):249-260, 1978.

In a paper presented at the Annual Meeting of the British Association for Psychopharmacology held in April 1978, brain specific benzodiazepine receptors are discussed with attention to their pharmacological characterization, their ontogenetic and phylogenetic development, temperature effects on binding, neuronal localization, and possible interaction with gamma-aminobutyric acid receptors. Brain membranes from rat and human contain a single class of brain specific binding sites for pharmacologically and clinically active benzodiazepines. There is good correlation between the pharmacological effects of benzodiazepines and the affinity for the diazepam binding site. Benzodiazepine binding sites are not present on glial cells. Flunitrazepam is a very suitable ligand for affinity binding and it binds to the same class of binding sites as diazepam. Results indicate that the in vitro diazepam and flunitrazepam binding sites are the receptors which (in vivo) mediate various pharmacological and clinical effects of benzodiazepines. 30 references. (Author abstract modified)

002055 Breese, George R.; Vogel, Richard A.; Kuhn, Cynthia M.; Mailman, Richard B.; Mueller, Robert A.; Schanberg, Saul M. Child Development Institute, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Behavioral and prolactin responses to 5-hydroxytryptophan in rats treated during development with 5,7-dihydroxytryptamine.** Brain Research (Amsterdam). 155(2):263-275, 1978.

The behavioral syndrome (rigidity, splayed feet, tremor, head weaving, salivation, and forepaw treading) typically induced by the serotonin precursor 5-hydroxytryptophan (5-HTP) was markedly potentiated in adult Sprague-Dawley rats treated intracisternally with 5,7-dihydroxytryptamine (5,7-DHT) during development. Prevention of the 5, 7-DHT-induced reduction of brain norepinephrine with pargyline or desipramine did not diminish the potentiation of 5-HTP, suggesting that noradrenergic fibers do not contribute to the altered 5-HTP response. Treatments with 5,7-DHT also potentiated the release of prolactin and the disruption of responding induced by 5-HTP in a fixed ratio operant task. Additional studies indicate that 5,7-DHT treatments potentiates 5-HTP without affecting the action of L-dihydroxyphenylalanine. Administration of the decarboxylase inhibitor RO-4-4602 at a dose that inhibits enzyme activity in brain blocked the 5-HTP-induced behavioral syndrome in 5,7-DHT treated rats, indicating that 5-HTP must be converted to serotonin for 5-HTP to alter behavior. It is concluded that destruction of serotonergic fibers during development can produce permanent changes in central serotonergic mechanisms. 37 references. (Autor abstract modified)

002056 Bridger, Wagner H.; Barr, Gordon A.; Gibbons, Judith L.; Gorelick, David A. Dept. of Psychiatry, Albert Einstein College of Medicine, Yeshiva University, Bronx, NY 10461 **Dual effects of LSD, mescaline and DMT.** In: Stillman, R.; The psychopharmacology of hallucinogens. New York, Pergamon, 1978. 338 p. (p. 150-180).

A paper read at the workshop on assessing hallucinogenic behavior sponsored by the Division of Research of the National Institute on Drug Abuse in Bethesda, Maryland, December 1976, is presented. On the basis of human data, it is proposed that hallucinogens have two effects: 1) the psychedelic effect which occurs in nonstressful situations and shows rapid tolerance and 2) the psychotomimetic effect, demonstrated only for d-lysergic acid diethylamide (LSD), which occurs in stressful situations and probably does not show tolerance. These two effects may have parallels in the animal behavior literature. LSD and mescaline typically have two effects on animal behavior: facilitation and disruption. Models for the psychotomimetic effect (the facilitatory effect) and for the psychedelic effect (the disruptive effect) are suggested. The effects of LSD and mescaline on biogenic amine systems and the effect of monoamine manipulations on both disruptive and facilitative effects are reviewed. It is concluded that these drugs affect all three amine transmitters and that catecholamine manipulations more often affect facilitative effects while 5-hydroxytryptamine manipulations more often affect disruptive effects. A weakness of this model is identified: some drugs which are not hallucinogenic also have dual effects on animal behavior. Furthermore, N,N-dimethyltryptamine (DMT) does not have facilitative effects. It is predicted that DMT might not have psychotomimetic effects. In addition, nonhallucinogenic analogues of mescaline do share mescaline's disruptive effects. This would suggest that the disruptive effects may not be a good model of psychedelic effects. 178 references.

002057 Brown, Roger M.; Crane, Alison M.; Goldman, Patricia S. Laboratory of Neuropsychology, NIMH, Bethesda, MD 20014 **Regional distribution of monoamines in the cerebral cortex and subcortical structures of the rhesus monkey: concentrations and in vivo synthesis rates.** Brain Research (Amsterdam). 168(1):133-150, 1979.

Endogenous monoamine concentrations and synthesis rates were examined in discrete regions of the cerebral cortex and subcortical structures of rhesus monkeys. Cortical monoamines showed topographically specific patterns of distribution. Dopamine was highest in the prefrontal and temporal neocortex, decreased along the fronto-occipital axis, and was present only in trace amounts in the visual cortex. Norepinephrine had a similar distribution, except that the highest concentration of norepin-

ephrine was found in the somatosensory cortex. Serotonin had a more uniform pattern of distribution, but the distribution of its metabolite, 5-hydroxyindoleacetic acid (5-HIAA), was complementary to that of dopamine; the 5-HIAA concentration was lowest in prefrontal cortex and highest in posterior regions of the telencephalon. Synthesis of the catecholamines generally paralleled the distribution of the catecholamines, but indoleamine synthesis was similar to the distribution of 5-HIAA. 99 references. (Author abstract modified)

002058 Buccafusco, J. J.; Brezenoff, H. E. Department of Pharmacology, College of Medicine and Dentistry of New Jersey, New Jersey Medical School, Newark, NJ 07103 **Pharmacological study of a cholinergic mechanism within the rat posterior hypothalamic nucleus which mediates a hypertensive response.** Brain Research (Amsterdam). 165(2):295-310, 1979.

In unanesthetized, freely moving male Sprague-Dawley rats, microinjection of cholinergic agonists into the posterior hypothalamic nucleus (PHN) consistently produced an elevation in mean arterial pressure (MAP). Microinjection of carbachol (0.1-100nmol) into the PHN elicited reproducible and dose related increases in MAP (17-47mm Hg) and variable changes in heartrate. Similar responses, but longer in onset and duration, were produced by microinjection of the cholinesterase inhibitors neostigmine, physostigmine, and echothiophate. The pressor responses produced by neostigmine and physostigmine, but not by carbachol, were dependent on intact stores of acetylcholine in the PHN. Blockade of muscarinic receptors by prior microinjection of atropine abolished the rise in MAP in response to subsequent injection of cholinergic agonists, but pretreatment with the antinicotinic agent, mecamylamine, was without effect. Intravenous injection of the alpha-adrenergic blocking agent, phentolamine, attenuated the pressor response to intrahypothalamic injection of carbachol or neostigmine. Results suggest that a muscarinic cholinergic mechanism in the rat PHN mediates the rise in MAP through an increase in sympathetic tone. 50 references. (Author abstract modified)

002059 Buice, R. G. College of Pharmacy, University of Tennessee Center for Health Sciences, Memphis, TN 38163 **Pharmacokinetics of pentobarbital in the barbital-dependent rat.** Research Communications in Psychology, Psychiatry and Behavior. 4(1):65-77, 1979.

The pharmacokinetics of intravenously administered pentobarbital were investigated in barbital dependent rats immediately upon withdrawal and 48 hours after withdrawal as well as in nondependent controls. Pentobarbital plasma concentration time course data from each group of rats is described by biexponential equation. In addition to the expected increase in pentobarbital plasma clearance rate and reduced biologic half-life, the volume of pentobarbital plasma distribution was reduced in rats that were withdrawn from barbital upon initiation of pentobarbital pharmacokinetic studies. Overall volumes of pentobarbital distribution, however, were not significantly affected at this point. In rats that had been withdrawn from barbital 48 hours prior to initiation of pentobarbital pharmacokinetic studies, there were reductions in the volume of plasma distribution as well as overall volumes of distribution. Since the 48 hour time point following withdrawan from barbital has been previously shown to be the time of maximum intensity for certain withdrawal effects, it is suggested that barbiturate withdrawal might have some influence on drug distribution. 17 references. (Author abstract)

002060 Bunney, B. S.; Grace, A. A. Dept. of Pharmacology and Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Acute and chronic haloperidol treatment: comparison of effects on nigral dopaminergic cell activity.** Life Sciences (Oxford). 23(16):1715-1727, 1978.

The effect of chronic subcutaneous haloperidol (CHAL) treatment (0.5mg/kg/day for 22 days) on nigral dopaminergic (DA) neuronal activity was examined in male Sprague-Dawley rats, using extracellular single unit recording and microiontophoretic techniques. CHAL treatment resulted in an almost total absence of spontaneously firing nigral DA cells. Silent DA cells became active when gamma-aminobutyric acid (GABA) or DA was applied microiontophoretically, but were unresponsive to glutamic acid. Intravenous apomorphine also caused the DA cells to fire. Destruction of the nigrostriatal feedback pathways by injection of kainic acid into the caudate nucleus prior to CHAL treatment prevented the disapperance of DA cell activity on the lesioned side. In animals treated acutely with haloperiodol, a significantly greater number of spontaneously firing DA cells were found than in controls. In control animals, inhibited DA cells could be activated by microiontophoretic glutamic acid or intravenous haloperidol, but not by GABA. Results are discussed in relation to the time dependent neurological side-effects induced by haloperidol and other antipsychotic drugs. 47 references. (Author abstract modified)

002061 Butt, Naeem M.; Collier, Harry O. J.; Cuthbert, Nigel J.; Francis, David L.; Saeed, Sheikh A. Miles Laboratories Ltd., Stoke Poges, Slough SL2 4LY, England **Mechanism of quasi-morphine withdrawal behaviour induced by methylxanthines.** European Journal of Pharmacology (Amsterdam). 53(4):375-378, 1979.

Seven phosphodiesterase inhibitors were tested for ability to induce a quasi morphine withdrawal syndrome (QMWS) in opiate naive, male Wistar rats. Five of the compounds induced a QMWS in a dose related fashion: 3-isobutyl-1-methyl-xanthine, 2-amino-6-methyl-5-oxo-4-n-propyl-4, 5-dihydro-5-triazolo(1,5-a)-pyrimidine, 4-(3-butoxy-4-methoxy-benzyl)-2-imidazolidone, theophylline, and caffeine, in descending order of potency. Their potencies in including a QMWS correlated significantly with those in inhibiting cyclic adenosine monophosphate phosphodiesterase but not cyclic guanosine monophosphate phosphodiesterase in rat brain homogenates. 8 references. (Author abstract modified)

002062 Buu, Nguyen T.; Kuchel, Otto. Clinical Research Institute of Montreal, 110 Pine Avenue West, Montreal, Quebec, H2W 1R7, Canada **The direct conversion of dopamine 3-0-sulfate to norepinephrine by dopamine-beta-hydroxylase.** Life Sciences (Oxford). 24(9):783-789, 1979.

Incubation of dopamine 3-0-sulfate (0.1mcmole) with purified bovine dopamine-beta-hydroxylase resulted in the formation of free norepinephrine (0.0073mcmole). The conversion to norepinephrine was inhibited by 0.6mM of fusaric acid, an inhibitor of dopamine-beta-hydroxylase. The reaction of dopamine 3-0-sulfate with dopamine-beta-hydroxylase followed Michaelis-Menten kinetics. The calculated Michaelis-Menten constant was 17mM, compared to 0.1mM for free dopamine. The incubation medium did not contain any sulfatase activity. 23 references. (Author abstract modified)

002063 Cantoni, G. L.; Chiang, P. K.; Skeel, A.; Leonard, E. J. NIMH, Bethesda, MD 20014 **Requirement of biological methylation for mouse macrophage phagocytosis. (Unpublished paper)** Bethesda, MD, NIMH, 1978. 1 p.

Macrophage phagocytosis was studied in the mouse. 3-Deazaadenosine (3-DZA), an inhibitor of adenosylhomocysteinase, at concentrations as low as .0000002M, inhibits phagocytic uptake of opsonized erythrocytes by monolayers of resident peritoneal macrophages. Inhibition of phagocytosis by 3-DZA is both dose and time dependent. The effects of 3-DZA are potentiated by simultaneous administration of L-homocysteine. These

observations imply that S-adenosylmethionine participates as a methyl donor in a reaction essential for the phagocytic response. The significance of this discovery is discussed. (Author abstract modified)

002064 Cantoni, Giulio L.; Richards, Henry H.; Chiang, Peter K. Laboratory of General and Comparative Biochemistry, National Institute of Mental Health, Bldg. 36, 3A19, Bethesda, MD 20014 **Inhibitors of S-adenosylhomocysteine hydrolase and their role in the regulation of biological methylation. (Unpublished paper).** Bethesda, MD, NIMH, 1978. 10 p.

An attempt to calculate what, on a percentage basis, might be the relative changes in the activities of a number of different enzymes at different AdoMet/AdoHcy ratios is presented. A large number of compounds, chemically related to AdoHcy and/or adenosine as inhibitors of AdoHcy hydrolase, were examined. Research was directed at using the inhibition of AdoHcy hydrolase in order to alter the intracellular level of AdoHcy and take advantage of underlying biological control mechanisms by amplifying it. It is demonstrated that it is possible to modify the intracellular ratio of AdoMet and AdoHcy and that these perturbations are important in the modulation of a variety of biological activities. 30 references.

002065 Cedarbaum, Jesse M.; Aghajanian, George K. Yale University School of Medicine and Connecticut Mental Health Center, 34 Park Street, New Haven, CT 06508 **Activation of locus coeruleus neurons by peripheral stimuli: modulation by a collateral inhibitory mechanism.** Life Sciences (Oxford). 23(13)1383-1392, 1978.

The response of 196 locus coeruleus (LC) units to sensory, peripheral nerve and antidromic stimulation was studied in 32 male Sprague-Dawley rats. Noradrenergic neurons of the rat locus coeruleus responded to noxious stimuli or peripheral nerve stimulation with a burst of spikes followed by a period of suppressed activity in which responses to additional stimuli were attenuated. A period of reduced activity, presumably mediated by inhibitory recurrent LC collaterals, followed antidromic activation of the LC. The supression of LC unit firing which follows nerve stimulation was reduced by piperoxane, and alpha adrenergic antagonist which is known to block the norepinephrine mediated autoinhibitory action of recurrent LC axon collaterals. The specificity of piperoxane in blocking norepinephrine was shown by the fact that it did not antagonize several other putative transmitters in the LC. It is concluded that the postactivation reduction of LC neuronal responsivity may be mediated in part through noradrenergic autoinhibitory mechanisms within the LC. 45 references. (Author abstract modified)

002066 Charlton, Clive G.; Way, E. Leong. Dept. of Pharmacology, University of California, San Francisco, CA 94143 **Tremor induced by S-adenosyl-L-methionine: possible relation to L-dopa effects.** Journal of Pharmacy and Pharmacology (London). 30(12):819-820, 1978.

In a letter to the editor, intraventricular administration of S-adenosyl-L-methionine (SAM) cause marked impairment of motor function in ICR mice is discussed. The dominant effect was tremor, and vigorous body shaking was observed with increasing doses. Impaired posture, spontaneous jumping, poverty of movement, and episodes of convulsions were also seen. The onset, latency, and duration of the SAM effects were dose dependent. The tremorgenic effects of SAM could be reversed by DL-dopa or cycloleucine. These findings suggest that a reduction in SAM may be related to the antiparkinson effect of L-dopa. 7 references.

002067 Chaturvedi, A. K.; Landon, E. J.; Sastry, B. V. Rama. State Toxicology Laboratory, P. O. Box 5195, North Dakota University School of Pharmacy, Fargo, ND 58102 **Influence of chlorpromazine on calcium movements and contractile responses of guinea-pig ileum longitudinal smooth muscle to agonists.** Arhcives Internationales de Pharmacodynamie et de Therapie (Ghent). 236(1):109-124, 1978.

The effects of chlorpromazine (CPZ) on the uptake and release of calcium by microsomes prepared from longitudinal smooth muscle of guinea-pig ileum in vitro and on contractions of longitudinal muscle of guinea-pig ileum in situ to various agonists were studied. CPZ blocked calcium uptake of the microsomes by 85% to 95%, and increased the release of preloaded calcium from the microsomes from 5% to 40% in the first 5 minutes. CPZ-induced calcium release was increased by chelating agents, KCl and NaCl. These agents increased the CPZ-induced calcium release from 40% in the first 5 minutes to an average of 87% in the first 5 minutes. It is concluded that CPZ appears to interfere at 1 to 10 micromole levels with calcium movements of the sarcolemma and in vitro at 0.5to 1 mM levels with calcium movements of isolated sarcoplasmic reticulum. 42 references. (Author abstract modified)

002068 Chau-Pham, Thuy T.; King, George; Dewey, William L. Department of Pharmacology, Meidcal College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Sodium-induced alterations of opiate effects on the binding of 3H-dihydromorphine to mouse brain homogenates.** Life Sciences (Oxford). 23(12):1293-1300, 1978.

Opiate effects on the stereospecific binding of 3H-dihydromorphine in mouse brain homogenates were investigated and compared with its effects on 3H-naloxone stereospecific binding on the guinea-pig ileum and its analgesic effects in man. The inhibitory potency of opiate agonists on the stereospecific binding of 3H-dihydromorphine in mouse brain homogenates was not affected by the presence of sodium ions. That of pure antagonists was greatly enhanced by sodium chloride whereas the inhibitory effects of mixed agonist antagonists were reduced by sodium chloride, indicating that sodium ions might affect the agonist component more than the antagonist component of narcotic antagonist analgesics. The inhibitory potency of the opiates tested agrees with their potency in reducing the stereospecific binding of 3H-naloxone to rat membranes, the contractions of coaxially stimulated guinea-pig ileum and their analgesic potency in animals and humans. 23 references. (Author abstract)

002069 Chavdarian, Charles G.; Karashima, Daiji; Castagnoli, Neal, Jr.; Hundley, Harvey K. Dept. of Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco, CA 94143 **Oxidative and cardiovascular studies on natural and synthetic catecholamines.** Journal of Medicinal Chemistry. 21(6):548-554, 1978.

The cyclic voltammometric behavior of epinephrine, norepinephrine, dopamine, epinine, alpha-methyldopamine, beta-methyldopamine, beta-methylepinine and beta-methoxyepinine was examined in order to evaluate substituent effects on cyclization rates of the electrochemically generated quinones. Alpha and beta substituents caused a modest enhancement of cyclization rates, while an N-methyl group dramatically increased cyclization rates. No correlation was observed between calculated amine pKa values, suggesting that differences in cyclization rates between the primary and secondary amine series were due to inherent nucleophilicity, a measure of which would be gas phase proton affinities. The acute pressor effects of the newly synthesized catecholamines were also compared with the native amines in the rat. 25 references. (Author abstract)

002070 Cheng, Hung-Yuan; Sackett, Patricia Holt; McCreery, Richard L. Department of Chemistry, Ohio State University

Columbus, OH 43210 , **Reactions of chlorpromazine cation radical with physiologically occurring nucleophiles.** Journal of Medicinal Chemistry. 21(9):948-952, 1978.

The reactions between the chlorpromazine cation radi al c and a variety of physiologically occurring nucleophiles, involving formation of a reversible covalent bond were examined. Results indicate that this reaction does not involve disproportionation of the radical, but is a direct reaction between radical and nucelophile. The resulting adduct further reacts to form chlorpromazine sulfoxide or hydroxylated derivatives, and the original nucleophile is regenerated. The products and kinetics of the reaction depend strongly on the identity of the nucleophile, with the sulfhydryl group being the fastest and water being the slowest of the nucleophiles studied. The involvement of these reactions in the metabolism of chlorpromazine is discussed, and it is suggested that radical/nucleophile interaction is a useful model reaction for the effects of chlorpromazine on neuronal enzymes and receptor sites. 19 references. (Author abstract modified)

002071 Chiflikyan, M. D.; Yesayan, N. A.; Manukhin, B. N. Laboratoriya biokhimii neyromediatorov Instituta biokhimii AN ArmSSR, Yerevan, USSR /**The effect of GABA on norepinephrine-H3 synthesis, uptake, and release from brain sections.**/ Deystviye GAMK na sintez, zakhvat i vykhod noradrenalina-H3 iz mozgovykh srezov. Fiziologicheskiy Zhurnal SSSR imeni I. M. Sechenova (Leningrad). 64(8):1097-1104, 1978.

Brain sections taken from rats were incubated in a physiological solution to test the effect of GABA introduction at different stages of incubation. GABA had no effect on the synthesis and uptake of norepinephrine-H3 (H3-NE) while increasing its loss from slices preincubated for 5 minutes before incubation for 30 minutes in the solution. When brain sections were preincubated for 30 minutes before addition of H3-NE, the effect of GABA on NE content in the sections was reversed. A similar reversal of the GABA effect occurred when the preincubation period of sections subjected to prolonged electrical stimulation was increased. The reversal did not correlate with the depletion of endogenous stores of NE, and may be due to the changes in the ionic composition of the brain sections in the course of the prolonged incubation. 24 references. (Journal abstract modified)

002072 Chrystal, Ewan; Bey, Philippe; Rando, Robert R. Department of Pharmacology, Harvard Medical School, 250 Longwood Avenue, Boston, MA 02115 **The irreversible inhibition of brain L-glutamate-1-decarboxylase by (2RS,3E)-2-methyl-3,4-didehydroglutamic acid.** Journal of Neurochemistry (Oxford). 32(5):1501-1507, 1979.

Incubation of chick embryo brain L-glutamate-1-decarboxylase (GAD) with (2RS,3E)-2-methyl-3,4-didehydroglutamic acid (MDG), a substrate analog of L-glutamic acid, resulted in a time dependent irreversible inhibition of enzyme activity. MDG is a substrate for GAD and required turnover prior to inactivating the enzymes; it was therefore classified as a kcat or suicide inhibitor. The inhibitor had no effect on the apoenzyme or the holoenzyme treated with hydrazine. L-glutamate and D-glutatamate, but not mercaptoethanol, reduced the rate of enzymic inactivation by MDG. The high specificity of this inhibitor should render it useful in studies of the physiological role of gamma-aminobutyric acid. 30 references. (Author abstract modified)

002073 Cohn, Dan F.; Axelrod, T.; Homonnai, Z. T.; Paz, G.; Streifler, M.; Kraicer, P. F. Department of Neurology, Ichilov Hospital and Medical Center, Weizman Ave., Tel-Aviv, Israel **Effect of diphenylhydantoin on the reproductive function of the male rat.** Journal of Neurology, Neurosurgery and Psychiatry (London). 41(9):858-860, 1978.

To study the effects of diphenylhydantoin on the reproductive function of the male rat, male albinos were injected with 5, 10, and 20mg diphenylhydantoin daily for 2 months and then caged for 5 days with cyclic females. Thereafter the males underwent necropsy; the organs of the genital tract were examined and found to be unaffected. Blood testosterone and Leydig cell counts were normal. A significant reduction of fertility was observed which appears to be loss of libido on behavioral grounds. Except for similar behavioral changes described in human epileptics, no further reports are available concerning anticonvulsants and fertility. Findings indicate that there is no reason to suspect that diphenylhydantoin has endocrine mediated effects on male fertility in the rat. 2 references. (Author abstract modified)

002074 Collingridge, G. L.; Davies, J. School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **An evaluation of D-alpha-aminoadipate and D-(and DL)alpha-aminosuberate as selective antagonists of excitatory amino acids in the substantia nigra and mesencephalic reticular formation of the rat.** Neuropharmacology (Oxford). 18(2):193-199, 1979.

The effects of microiontophoretically applied D-alpha-aminoadipate (DAA) and a higher homologue D-(and DL)alpha-aminosuberate on responses to excitatory amino acids and acetylcholine (ACh) in single cells in the rat substantia nigra and overlying mesencephalic reticular formation were investigated. Both compounds reversibly reduced or abolished responses to the amino acids, but had no effect on ACh. Responses to N-methyl-D-aspartate were always reduced to a greater extent than were responses to kainate, and responses to L-aspartate were usually reduced more rapidly than responses to L-glutamate. DAA had no effect on responses to microiontophoretically applied substance-P, and neither antagonist reduced the short latency excitation of nigral cells evoked by electrical stimulation of the ipsilateral striatum. 38 references. (Author abstract modified)

002075 Colpaert, F. C. Dept. of Pharmacology, Janssen Pharmaceutica, B-2340 Beerse, Belgium **Long-term suppression of pain by narcotic drugs in the absence of tolerance development.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 236(2):293-295, 1978.

The responsivity to an acute nociceptive stimulus and the analgesic response to the long acting narcotic analgesic bezitramide were investigated in rats that had been exposed to an experimental model of chronic pain. It was found that 1) exposure to chronic pain which is associated with Mycobacterium-induced adjuvant arthritis induces a hypoalgesia which can be attenuated by chronic narcotics administration, 2) chronic narcotic administration narcotic administration induces a hyperalgesia which can be attenuated by chronic pain, and 3) the tolerance to narcotic analgesia which otherwise develops upon chronic narcotic administration may fail to occur in animals exposed to chronic pain. It is suggested that a new hypothesis on pain processing by the central nervous system may be viable and that chronic pain can be treated effectively. 4 references.

002076 Corcoran, Michael E.; Wada, Juhn A. Dept. of Psychology, University of Victoria, P. O. Box 1700, Victoria, BC, Canada V8W 2Y2 **Naloxone and the kindling of seizures.** Life Sciences (Oxford). 24(9):791-795, 1979.

The effect of naloxone (20 or 40mg/kg ip) on the kindling of seizures by repeated electrical stimulation of the amygdala or the caudate nucleus was investigated in male Long-Evans hooded rats. Naloxone had no effect on the threshold for local afterdischarge in the two areas and failed to retard the rate of

kindling of clinical seizures. Results suggest that an interaction of endogenous opioid peptides with central opiate receptors does not play a critical role in the kindling of seizures. 29 references. (Author abstract modified)

002077 Costa, E.; Cheney, D. L.; Mao, C. C.; Moroni, F. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Action of antischizophrenic drugs on the metabolism of gamma-aminobutyric acid and acetylcholine in globus pallidus, striatum and n. accumbens.** Federation Proceedings. 37(10):2408-2414, 1978.

At the Annual Fall Meeting of the American Society for Pharmacology and Experimental Therapeutics held in Columbus, August 23, 1977, a paper was presented in which the action of classical and atypical antipsychotic drugs on the turnover rate of gamma-aminobutyric acid and acetylcholine in the brain nuclei of rats is investigated. The data suggest that the increase in the turnover rate of acetylcholine in n. accumbens and striatum caused by the classical antischizophrenic drugs cannot be taken as a biochemical marker of their symptomatic relief of schizophrenia. It is suggested that the increase in metabolism of gamma-aminobutyric acid in nigra and n. caudatus caused by atypical antipsychotics might be a biochemical correlate that explains why these drugs, although they block dopamine receptors, fail to cause tardive dyskinesia or extrapyramidal side-effects. It has been observed that the increase in turnover rate of gamma-aminobutyric acid in n. accumbens persists after chronic haloperidol or clozapine, suggesting that this change could be a biochemical marker for the mechanisms involved in the symptomatic relief of schizophrenia elicited by these two antischizophrenic drugs. 48 references. (Author abstract modified)

002078 Costa, E.; Guidotti, A.; Toffano, G. Laboratory of Preclinical Pharmacology, National Institute of Mental Health, Saint Elizabeths Hospital, Washington, D. C. 20032 **Molecular mechanisms mediating the action of diazepam on GABA receptors.** British Journal of Psychiatry (London). 133(September):239-248, 1978.

Molecular mechanisms mediating the action of diazepam on gamma-aminobutyric acid (GABA) receptors are discussed in a paper presented to the Annual Meeting of the British Association for Psychopharmacology held on April 7, 1978. Preparation of two types of crude synaptic membranes which differ in their kinetic properties to bind labelled GABA in a NA free medium is reported: type A has two populations of receptors with a high and a low affinity for GABA binding, type B has one type of receptor with a low affinity. This difference is due to the presence of a selective endogenous inhibitor of the high affinity receptor for GABA, a thermostable protein of about 15,000 molecular weight. A number of psychopharmacological studies of effects of diazepam, clonazepam, chlordiazepoxide, and two enantiomers of a benzodiazapine on the endogenous inhibitor are reported. The endogenous protein inhibitor was also found to competitively block high affinity binding of labelled diazepam to type A membranes. Findings indicate that the endogenous inhibitor and diazepam act on the same receptor, and that the endogenous inhibitor may be a natural ligand for brain receptors that bind benzodiazepines with high affinity. 27 references. (Author abstract modified)

002079 Costall, B.; Fortune, D. H.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, West Yorkshire, England **Involvement of mesolimbic and extrapyramidal nuclei in the motor depressant actin of narcotic drugs.** Journal of Pharmacy and Pharmacology (London). 30(9):566-572, 1978.

The ability of narcotic drugs to induce motor depression from the mesolimbic nucleus accumbens (ACB) and extrapyramidal caudate-putamen (CP) was investigated using the bilateral intracerebral injection technique. Drugs were injected alone in the ACB or CP and catalepsy was assessed,and then drugs were injected peripherally and intracerebrally to determine their ability to antagonize the marked hyperactivity induced by intraACB dopamine in the presence of nialamide. It is suggested that the ACB, and not the CP, is the site at which morphine acts to cause motor depression, while other narcotic drugs are able to act in both areas. In constrast, the neuroleptic fluphenazine appears to differentially affect motor function via the ACB and CP, antagonizing a dopamine hyperactivity in the former and primarily inducing catalepsy from the latter nucleus. 20 references. (Author abstract modified)

002080 Cote, Thomas E.; Kebabian, John W. Biochemical Neuropharmacology Unit, Experimental Therapeutics Branch, NINCDS, NIH, Bethesda, MD 20014 **Beta-adrenergic receptor in the brain: comparison of 3H-dihydroalprenolol binding sites and a beta-adrenergic receptor regulating adenylyl cyclase activity in cell free homogenates.** Life Sciences (Oxford). 23(16):1703-1713, 1978.

Specific tritiated dihydroalprenolol binding sites showed properties similar to those of the beta-adrenergic receptor regulating adenylyl cyclase activity in a homogenate of female New Zealand rabbit cerebellum. The rabbit cerebellum had 5 to 6pmole/g high affinity specific binding sites for 3H-dihydroalprenolol. The interaction of several beta-adrenergic agonists and antagonists with the specific binding sites was rapid, reversible, and stereospecific. Beta-adrenergic agonists showed a similar potency as agonists of adenylyl cyclase activity and as inhibitors of 3H-dihydroalprenolol binding (1-isoproterenol, 1-epinephrine, and 1-norepinephrine, in descending order of potency). The binding affinities of several beta-adrenergic agonists and antagonists for the specific binding sites approximated the affinities of these compounds for the stimulation of adenylyl cyclase. 17 references. (Author abstract modified)

002081 Cox, B. M.; Ross, Maureen; Goldstein, Avram; Palmour, Roberta M. Addiction Research Foundation, Palo Alto, CA **Pharmacological and immunological characterization of the Leu5 analogue of human beta-endorphin.** Brain Research (Amsterdam). 165(2):311-319, 1979.

The potencies of human beta-endorphin (Bh-endorphin), Met(0)5-Bh-endorphin, and synthetic Leu5-Bh-endorphin were compared in three bioassays of opioid activity and in two radioimmunoassays. In all assays, a peptide isolated from hemodialysates from a psychotic patient behaved like Leu5-Bh-endorphin. Leu-5-Bh-endorphin had only 20% the potency of Bh-endorphin in guinea pig ileum myenteric plexus, but was only sightly less active than Bh-endorphin in mouse vas deferens and in the guinea pig brain opiate receptor binding assay. The low cross-reactivity of Leu5-Bh-endorphin relative to Bh-endorphin with an antiserum to beta-endorphin suggests that the preferred solution condormations of these peptides are different. In all bioassays, Bh-endorphin was 2-3 fold less potent than camael beta-endorphin. 20 references. (Author abstract modified)

002082 Cutler, R. W. P.; Young, J. Dept. of Neurology, Stanford University School of Medicine, Stanford, CA 94305 **Bidirectional movement of gamma-aminobutyric acid in cerebral cortex slices incubated in small volumes of medium.** Brain Research (Amsterdam). 165(2):261-270, 1979.

Sprague-Dawley rat cortex slices were incubated in small volumes of medium to study the bidirectional movement of gamma-aminobutyric acid (GABA) between tissue and medium. The

extent of release of endogenous amino acids was dependent on the amino acid, the duration of incubation, and the volume of incubating medium. Comparison of apparent uptake, real uptake, and net change in GABA indicated that the accumulation of endogenous GABA may affect the calculation of GABA uptake when this is based on the initial specific activity of exogenous 14C-labeled GABA. The difference between apparent uptake and real uptake was particularly prominent in the presence of the depolarizing agents potassium and veratridine, which caused a marked increase in GABA release. Exchange or net release of GABA was observed when slices were incubated briefly in media containing 1.3mcM or 12.5mcM exogenous GABA; net uptake accounted for 50% of observed uptake when slices were incubated in media containing 25mcM GABA. 18 references. (Author abstract modified)

002083 Davis, Stephen F.; Prytula, Robert E. Austin Peay State University, Clarksville, TN 37040 **Odor-mediated runway performance of the rat as a function of Thorazine injection.** Bulletin of the Psychonomic Society. 13(5):293-296, 1979.

The influence of Thorazine on the production and utilization of odors was studied in rats. Two groups of runway trained rats received a double alternation sequence of reward/nonreward in a straight runway in the presence of odors exuded by startbox donors injected with Thorazine and saline, respectively. Appropriate start and run measure patterning was initially displayed only when the donors were saline injected. However, reversing the donor injected condition resulted in the development of such patterning by the subjects having donors shifted from Thorazine to saline, and the maintenance of patterning by the subjects having donors shifted from saline to Thorazine. 11 references. (Author abstract modified)

002084 de Montigny, Claude; Aghajanian, George K. Centre de Recherche en Sciences, Neurologiques, Faculte de Medecine, Universite de Montreal, Montreal, Canada H3C 3T8 **Tricyclic antidepressants: long-term treatment increases responsivity of rat forebrain neurons to serotonin.** Science. 202(4374):1303-1306, 1978.

Evidence is presented that long-term treatment of rats with clinically effective tricyclic antidepressant drugs induces a selective increase in the inhibitory response of forebrain neurons to serotonin applied by microiontophoresis. Long-term administration of some related drugs which lack antidepressant efficacy failed to induce such a change. The enhanced response to serotonin induced by the clinically active tricyclic drugs took 1 to 2 weeks to develop, a time course which correlates with the delayed onset of therapeutic effects in humans. 39 references. (Author abstract)

002085 De Souza, Helenice; Trajano, Eleonora; deCarvalho, Fernando Varela; Palermo Neto, Joao. Laboratory of Therapeutics, Faculty of Veterinary Medicine, University of Sao Paulo, Sao Paulo, Brasil **Effects of acute and long-term cannabis treatment on restraint-induced gastric ulceration in rats.** Japanese Journal of Pharmacology (Kyoto). 28(3):507-510, 1978.

The effects of Cannabis sativa extract (CE) treatment upon restraint induced gastric ulceration in Wistar rats were investigated to determine the possible relationships among the schedule of CE administration, dose of CE administered and immobilization induced gastric lesions. Although administration of 5, 10, and 20mg/kg of CE increased the degree of ulceration in restrained rats, doses of 40.0and 60mg/kg had a protective effect on immobilization-induced gastric lesions, reducing ulceration to below levels for restrained rats treated with saline and saline plus Tween-80. Long-term CE treatment in unrestrained animals at 60mg/kg dose level induced gastric lesions. 16 references.

002086 DeFraites, E. G.; van Kammen, D. P.; Bunney, W. E., Jr. National Institute of Mental Health, Bldg. 10, 4N-214, 9000 Rockville Pike, Bethesda, MD 20014 **Acute neuroendocrine effects of gamma-hydroxy butyrate. (Unpublished paper).** Bethesda, MD, NIMH, 1978. 1 p.

Gamma-hydroxy butyrate (GHB), a drug reported to inhibit the firing rate of nigrostriatal dopamine neurons, was given to four males and two females in doses of 2g or 4g. With the patients at bedrest, serial blood samples for hormone determinations were drawn. Prolactin rises 60 minutes after acute GHB, returns to baseline at about 180 minutes, then falls below baseline. In the male group, statistical significance was reached in the elevations of prolactin at 90 and 120 minutes and the decline in prolactin at 240 minutes. The pattern in the two females was similar. Growth hormone showed elevations in all patients but in an irregular pattern. Time of peak GH elevation occurred during the time/period of prolactin elevation. The implications of the results for GHB's mechanism of action in ongoing trials of the drug in schizophrenia are discussed. (Author abstract modified)

002087 Di Chiara, G.; Morelli, M.; Porceddu, M. L.; Gessa, G. L. Institute of Pharmacology, University of Cagliari, 09100 Cagliari, Italy **Evidence that nigral GABA mediates behavioural responses elicited by striatal dopamine receptor stimulation.** Life Sciences (Oxford). 23(20):2045-2052, 1978.

Evidence is presented that bilateral intranigral administration of GABA receptor blockers (pictrotoxin or bicuculline) elicits catatonia not surmountable by administration of apomorphine, a dopamine (DA) receptor agonist. Unilateral intranigral administration of GABA receptor blockers ipsilateral to a lesion of nigrostriatal DA neurons induced with 6OH-DA, antagonizes the contralateral turning produced by apomorphine. Results indicate that behavioral responses elicited by striatal DA receptor stimulation are effected through a GABA mediated inhibition of pars reticulata neurons. 15 references. (Author abstract)

002088 Dingledine, Raymond; Gjerstad, Leif. Dept. of Pharmacology, School of Medicine, University of North Carolina, Chapel Hill, NC 27514 **Penicillin blocks hippocampal IPSPs, unmasking prolonged EPSPs.** Brain Research (Amsterdam). 168(1):205-209, 1979.

Intracellular recordings from CA1 pyramidal cells in transverse slices of the guinea pig hippocampus indicated that penicillin blocked the conductance of increase associated with recurrent inhibitory postsynaptic potentials (IPIPs). Concurrent with IPSP reduction, the mixed excitatory postsynaptic potential/IPSP elicited by weak afferent stimulation was converted to a larger and more prolonged depolarizing potential. In this way, penicillin elevated the firing probability to a constant orthodromic stimulus and raised the excitability of the pyramidal cell population. 20 references.

002089 Dohi, T.; Tsujimoto, A. Dept. of Pharmacology, Hiroshima University School of Dentistry, Kasumi, Hiroshima, Japan. **Possible mechanisms of sustained tremor induction by nicotine in pilocarpine treated animals.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 235(1):62-72, 1978.

In male Wistar rats with sustained tremor evoked by nicotine and pilocarpine, the norepinephrine content of several brain regions was decreased, while striatal dopamine content was unchanged. Homovanillic acid concentrations were slightly increased, while 5-hydroxyindoleacetic acid concentrations were markedly increased. Pilocarpine alone increased the 5-hydroxytryptamine (5-HT) turnover rate at high ambient temperature but not at normal ambient temperature; atropine partially blocked the pilocarpine-induced increase in 5-HT turnover rate.

Pretreatment with p-chlorophenylalanine and hemicholinium-3 decreased the intensity of tremors elicitd by nicotine and pilocarprine. 31 references. (Author abstract modified)

002090 Dolphin, A.; Jenner, P.; Marsdem C. D. Groupe NB, Inserm U114, College of France, 11 Place Marcelin Berthelot, Paris Cedex 05, France **3-Methoxy-4-hydroxyphenylglycol sulphate (MOPEG-S04) as an index of cerebral noradrenaline turnover following depletion of transmitter stores in the rat.** Journal of Pharmacy and Phramacology (London). 30(9):580-582, 1978.

The hypothesis that central noradrenergic neurons can release and metabolize noradrenaline at a normal rate despite synthesis blockade, so long as adequate stores of the amine are available was investigated by examining cerebral concentrations of 3-methoxy-4-hydroxyphenylglycol sulphate (MOPEG-SO4) as an index of cerebral noradrenaline turnover following a range of procedures designed to cause a variable reduction in cerebral noradrenaline concentrations. Stored noradrenaline was depleted using reserpine and its synthesis was inhibited with alpha-methyl-p-tyrosine and the bis-1-methyl-4-homopiperazinyl-thiocarbonyl disulphide (FLA-63). Results indicate that when brain noradrenaline concentration is reduced, MOPEG-SO4 values are maintained and afford a better index of neuronal activity than measurement of the transmitter itself. 16 references.

002091 Domer, Floyd R.; Llera, Juan-Carlos. Department of Pharmacology, 1430 Tulane Avenue, New Orleans, LA 70112 **Blood-brain barrier permeability changes caused by lead exposure and amphetamine in mice.** Research Communications in Psychology, Psychiatry and Behavior. 3(2):101-108, 1978.

An experiment was performed with mice to determine whether lead exposure alters the blood-brain barrier (BBB) permeability and whether this alteration is affected by the administration of amphetamine. The drinking water of pregnant CD-1 mice was changed either to 0.5% sodium acetate or 0.5% lead acetate from the time of delivery of the offspring. The pups were weaned at 21 days of age and maintained on the same drinking solutions. Bodyweight, locomotor activity and BBB permeability were evaluated when the mice were 35-45 days of age. The lead exposed mice were smaller and hyperactive relative to the sodium exposed controls. The BBB permeability was also increased, but not significantly. When amphetamine (3mg/kg i.p.)was given it significantly decreased the BBB permeability only in the lead exposed mice. It is suggested that decreased BBB permeability caused by amphetamine medication explains the latter's utility in treating adolescent hyperactivity. 25 references. (Author abstract modified)

002092 Drewnowski, Adam; Grinker, Joel A. Dept. of Psychology, University of Toronto, Toronto, Ontario M5S 1A1, Canada **Food and water intake, meal patterns and activity of obese and lean Zucker rats following chronic and acute treatment with delta9-tetrahydrocannabinol.** Pharmacology Biochemistry and Behavior. 9(5):619-630, 1978.

A series of experiments investigating the effects of delta9-tetrahydrocannabinol (delta9-THC) on food and water intakes and wheel running activity of Zucker rats is described. Following chronic drug treatment (15 days), food and water intakes of all rats were suppressed, but intakes and body weights of the obese rats recovered more slowly than those of lean rats. Acute effects of the drug (24 hrs) were examined using techniques of meal pattern analysis and are discussed in relation to known patterns of anorectic drug action. Drug-induced anorexia was both delayed and of short duration, with no rebound eating observed for either solid or liquid diets. The time course of the suppression of feeding was paralleled by a suppression in running wheel activity. These findings suggest that the drug-induced reduction in food and water intake may be the result of a decreased level of arousal. 30 references. (Author abstract modified)

002093 Dudai, Yadin. Department of Neurobiology, Weizmann Institute of Science, Rehovot, Israel **Modulation of benzodiazepine binding sites in calf cortex by an endogenous factor and GABAergic ligands.** Brain Research (Amsterdam). 167(2):422-425, 1979.

The specific binding of tritiated flunitrazepam (3H-FNZ) to homogenate and membrane preparations from calf cortex at 37 degrees centigrade indicated that binding to membranes is modulated by a supernatant factor as well as by gamma-aminobutyric acid (GABA) like ligands. Although 3H-FNZ specifically bound to calf cortex homogenate and to washed membrane preparations from calf cortex, the dissociation constants for the two preparations were significantly different, indicating that a factor removed from the membranes during washing increases the affinity of the particulate binding sites toward 3H-FNZ. A similar modulation of 3H-FNZ binding site affinity in washed membranes was obtained by addition of GABA or the GABA agonist d,1-trans-3-aminocyclopentane carboxylic acid. Results indicate that the in vitro affinity of benzodiazepine binding sites at physiological temperature depends on an endogenous ligand that may be washed out. It is suggested that benzodiazepine binding sites may be modulated by activators and inhibitors, both of which may be related to GABA mechanisms. 11 references.

002094 Ebstein, R. P.; Hermoni, M.; Belmaker, R. H. Ezrath Nashim Mental Hospital, Jerusalem, Israel **Effect of lithium on cyclic AMP accumulation in rat brain.** Israel Journal of Medical Sciences (Jerusalem). 14(9):997-998, 1978.

A summary of a paper read at the 41st Meeting of the Israel Physiological and Pharmacological Society held March 1978, in Jerusalem is presented. Noradrenaline (NA) stimulated accumulation of cyclic APM (cAMP) in a resuspended rat cortical P2 pellet in the presence and absence of lithium (Li) was investigated. Both 2mM and 5mM Li significantly inhibit the Na stimulated accumulation of cAMP. In the presence of a phosphodiesterase inhibitor, Li still significantly inhibits NA-induced accumulation of cAMP, demonstrating that the inhibitory action of Li is not mediated by phosphodiesterase. In order to distinguish between the effect of Li on the cortical alpha and beta-receptor, L-isoproterenol stimulated accumulation of cAMP was examined. Both 2mM and 5mM Li significantly inhibit the beta-adrenergic stimulated accumulation of cAMP. The effect of Li was also examined on Na-induced accumulation of cAMP in cortical slices. Both 2mM and 3mM Li significantly inhibit cAMP accumulation after maximal neurohormonal stimulation. At low Li concentrations the effect of Li on basal cAMP accumulation in the absence of exogenous NA is stimulatory. (Author abstract modified)

002095 Ebstein, Richard P.; Reches, Avinoam; Belmaker, Robert H. Jerusalem Mental Health Center-Ezrat Nashim, P.O. Box 140, Jerusalem, Israel **Lithium inhibition of the adenosine-induced increase of adenylate cyclase activity.** Journal of Pharmacy and Pharmacology (London). 30(2):122-123, 1978.

The effects of lithium on the adenosine stimulated accumulation of cyclic 3',5'-adenosine monophosphate (cAMP) was investigated using crude synaptosome preparations from guinea pig cortex and caudate nucleus. Lithium produced a dose dependent inhibition of the adenosine stimulated increase in cAMP levels in both brain areas. At higher concentrations of lithium, the caudate nucleus was significantly more sensitive to lithium than was the cortex. The combined effect of adenosine and norepinephrine (NE) on cAMP concentrations in guinea pig cortex

was also examined. The effects of adenosine and NE were additive, suggesting that separate receptors exist for each of these compounds. It is suggested that until the role of adenosine in neurotransmission becomes more defined, the significance of the lithium effect on adenosine stimulated cAMP accumulation cannot be evaluated. However, it is pointed out that if adenosine plays a modulating role in neurotransmission by interacting with neurotransmitter specific adenylate cyclases, as has been suggested, then the inhibitory effect of lithium may be an integral part of its action in mania. 17 references.

002096 Elliott, J. M.; Glen, J. B. M. R. C. Clinical Pharmacology Unit, Radcliffe, Infirmary, Oxford, England **The effects of some analgesic and neuroleptic drugs on the spasmogenic actions of substance P on guinea-pig ileum.** Journal of Pharmacy and Pharmacology (London). 30(9):578-579, 1978.

The effects of some analgesic and neuroleptic drugs on the spasmogenic actions of substance-P on guinea-pig ileum were investigated to explore the hypothesis that the analgesic activity of certain compounds results for substance-P antagonist activity. At concentrations up to 10 micromoles, the peripherally acting analgesics indomethacin, paracetamol, ketoprofen, naproxen, and ibuprofen failed to antagonize the contractions to substance-P. Naloxone, morphine, codeine, pethidine, and diethylthiambutene were similarly ineffective. Phenoperidine and fentanyl both caused reversible inhibition of the response to substance-P. In acetic acid solution of the butyrophenones haloperidol, pimozide, and droperidol all caused irreversible inhibition of the response to substance-P. 11 references.

002097 Elliott, P. N. C.; Jenner, P.; Marsden, C. D. School of Pharmacy, Liverpool Polytechnic, Byrom Street, Liverpool L3 3AF, England **Atropine manipulation of elevated cerebral dopamine turnover caused by haloperidol or substituted benzamide drugs.** Journal of Pharmacy and Pharmacology (London). 30(12):788-791, 1978.

The effects of atropine on the increase in dopamine turnover produced by haloperidol or substituted benzamide drugs in male Swiss mice were examined. Sulpiride (50mg/kg), clebopride (10mg/kg), metoclopramide (20mg/kg), tiapride (50mg/kg), tigan (200mg/kg), and haloperidol (0.1mg/kg) all produced an increase in striatal and mesolimbic homovanillic acid (HV) and 3,4-dihydroxyphenylacetic acid (DOPAC) concentrations. Sultopride (10mg/kg) increased striatal and mesolimbic HVA concentrations, but did not alter DOPAC concentrations. Atropine partially reversed the increase in HVA induced by sulpiride or haloperidol, but did not affect DOPAC levels. Atropine did not rverse the effects of clebopride on HVA and DOPAC and did not reverse the HVA increase induced by metoclopramide. Atropine reversed the increase in mesolimbic DOPAC induced by tiapride, but did not alter tiapride effects on HVA. Atropine did not reverse the increase in HVA concentrations induced by sultopride, but the combination of atropine and sultopride resulted in increased striatal DOPAC concentrations. Atropine abolished or markedly reduced the increase in DOPAC and HVA induced by tigan. Results indicate that most substituted benzamide drugs differ from classic neuroleptics such as haloperidol by acting on cerebral dopamine pathways that are not balanced by cholinergic input. 28 references.

002098 Emson, P. C. MRC Neurochemical Pharmacology Unit, Department of Pharmacology, Medical School, Cambridge, England **Complementary disturbution of dopamine, substance P, and acetylcholine in the rat prefrontal cortex and septum.** Advances in Biochemical Psychopharmacology. 19:397-400, 1978.

The coexistence of substance-P, dopaminergic, and cholinergic transmitter systems within the prefrontal cortex was demonstrated in rats using radioimmunoassay, histological, and immunohistochemical techniques. These three transmitters have also been shown to coexist in the amygdala, nucleus accumbens, and olfactory tubercle. These findings suggest that the prefrontal cortex should be considered part of the limbic system. 16 references.

002099 Emson, P. C.; Paxinos, G.; Le Gal La Salle, G.; Ben-Ari, Y.; Silver, Ann. MRC Neurochemical Pharmacology Unit, Department of Pharmacology, Cambridge CB2 2QD, England **Choline acetyltransferase and acetycholinesterase containing projections from the basal forebrain to the amygdaloid complex of the rat.** Brain Research (Amsterdam). 165(2):271-282, 1979.

The origin of the cholinergic innervation to the amygdaloid complex was studied in male Wistar rats, using acetylcholinesterase (AChE) histochemistry and choline acetyltransferase (ChAT) assay of microdissected nuclei. The AChE positive neurons in central forebrain were distributed in a continuous system from the septum through the lateral preoptic area, to the entopeduncular nucleus caudally. Knife cuts or kainic acid lesions in the lateral preoptic area resulted in substantial depletion of AChE and ChAT in the amygdala. Kainic acid injections in the diagonal band area or cuts through the stria terminalis dorsally did not significantly modify AChE or ChAT in the amygdala, but the diagonal band injections partially depleted hippocampal ChAT. Parasaggital knife cuts undercutting the lateral pyriform cortex also failed to modify the AChE and ChAT content of the amygdala, but they depleted the undercut cortex of both enzymes; AChE positive material accumulated ventrally and medially to the knife cut. It is suggested that the major sources of the cholinergic innervation of the amygdala are the magnocellar AChE positive neurons in the lateral preoptic area and adjacent regions of the ventral forebrain. 23 references. (Author abstract modified)

002100 Engel, J.; Ahlenius, S.; Almgren, O.; Carlsson, A.; Larsson, K.; Sodersten, P. Dept. of Pharmacology, University of Goteborg, Fack, S-40033 Gothenburg, Sweden **Effects of gonadectomy and hormone replacement on brain monoamine synthesis in male rats.** Pharmacology Biochemistry and Behavior. 10(1):149-154, 1979.

The synthesis of catecholamines and serotonin in the brains of castrated male Wistar rats was analyzed at various times after castration and at various ages. Castration of rats of 50 days of age or later caused an increase in brain monoamine synthesis, but this phenomenon was not observed until 20 days after castration. The increase in brain monamine synthesis following castration was counteracted by treatment with testosterone. Results suggest that testosterone exerts an inhibitory influence on monoamine synthesis. 40 references. (Author abstract modified)

002101 Enright, James T. University of California, San Diego, CA 92037 **The paradox of the pineal in circadian rhythms. (Unpublished paper).** Final Report, NIMH Grant MH-29331, 1978. 7 p.

The hypothesis that the pineal gland is the master circadian rhythm generator in birds was challenged, on the basis of evidence that the house sparrow used in previous research is an atypical subject. The house finch, a species whose circadian rhythms are markedly less sensitive to constant light, was instead used, and it was proposed that the pineal does not serve as a rhythm generator, but rather provides only a component of permissive conditions for a pacemaker system located elsewhere. The effects of deuterium on pinealectomized birds were also determined. Ss were administered melatonin, a major pineal

hormone, and were tested to determine if it would restore the rhythms if given in chronically implanted silastic capsules. The results show similar activity patterns among house finches and those reported for the house sparrow, and rhythmicity in constant darkness was not restored by i.p. melatonin capsules. In addition, deuterium added to drinking water did not restore rhythmicity.

002102 Evans, R. H. Department of Pharmacology, Medical School, University Walk, Bristol BS8 1TD, England **Cholinoceptive properties of motoneurones of the immature rat spinal cord maintained in vitro.** Neuropharmacology (Oxford). 17(4/5):277-279, 1978.

The presence of muscarinic cholinoceptors in motoneurones of the immature rat spinal cord maintained in vitro was demonstrated. Threshold depolarizing responses, recorded from the ventral root of the isolated hemisected spinal cord, were obtained at 1mcM carbachol; these responses were specifically antagonized by atropine (50nM). Neostigmine (1mcM) potentiated responses to acetylcholine in the presence of tetrodotoxin (0.1mcM). In the absence of tetrodotoxin, neostigmine produced a depolarization of motoneurons, indicating the release of acetylcholine from nerve terminals within the preparation. 13 references. (Author abstract modified)

002103 Fekete, M. I. K.; Kanyicska, B.; Herman, J. P. Institute of Experimental Medicine, Hungarian Academy of Sciences, 1450 Budapest, Hungary **Simultaneous radioenzymatic assay of catecholamines and dihydroxy-phenylacetic acid (DOPAC); comparison of the effects of drugs on the tuberoinfundibular and striatal dopamine metabolism and on plasma prolactin level.** Life Sciences (Oxford). 23(15):1549-1556, 1978.

A simultaneous radioenzymatic assay for catecholamines and dihydroxy-phenylacetic acid (DOPAC) was developed. Tritiated methoxy amine and homovanillic acid formed in the presence of tritiated S-adenosyl-methionine and catechol-O-methyltransferase were separated by organic solvent extraction and chromatography. Chlorpromazine and haloperidol (but not supriride) increased the DOPAC content in the striatum, without affecting the DOPAC level in the median eminence. Gamma-butyrolactone also increased the dopamine content only in the striatum. The monoamine oxidase inhibitor pargyline decreased the DOPAC level in both areas examined. All the drugs tested increased plasma prolactin level. Results suggest that the biochemical responses of nigrostriatal and tuberoinfundibular dopaminergic neurons may not be analogous. 23 references. (Author abstract modified)

002104 Fernstrom, Madelyn Hirsch; Wurtman, Richard J. Laboratory of Neuroendocrine Regulation, Dept. of Nutrition and Food Sciences, Massachusetts Institute of Technology, Cambridge, MA 02139 **Increase in striatal choline acetyltransferase activity after choline administration.** Brain Research (Amsterdam). 165(2):358-361, 1979.

Caudate choline acetyltransferase (CAT) activity was significantly (27%) elevated 8 hours after intragastric choline chloride (ChCl) administration to male Sprague-Dawley rats and remained high after 24 hours. The choline and acetylcholine (ACh) contents of the caudate nucleus were also elevated 8 hours after ChCl, but not after 24 hours. Brain CAT activity and choline and ACh levels returned to control levels within 48 hours of ChCl administration. The Michaelis-Menten constant of CAT for choline was slightly increased in ChCl treated animals, and the maximum velocity of CAT was increased by 69% 8 hours after ChCl and by 35% 24 hours after administration of the precursor. These findings indicate that even a large and prolonged increase in brain ACh levels causes no simultaneous reduction in CAT activity. It is concluded that cholinergic neurons can exert positive, but not negative, feedback on themselves and the structures they innervate. 27 references.

002105 Fludder, Joan M.; Tonge, Sally R. Dept. of Pharmacology, University College, Galway, Northern Ireland **The interaction between female sex hormones and d-amphetamine on central biogenic amines during the rat oestrous cycle.** Irish Journal of Medical Science (Dublin). 147(Supplement 1):28-32, 1978.

A paper read at the first Irish Psychopharmacology Conference, held in Belfast in March 1978, is presented. The effects of d-amphetamine on catecholamine concentrations in the amygdaloid and hypothalamic regions of rat brain during the estrous cycle were investigated. The response to amphetamine varied according to the stage of the estrous cycle at the time of administration. At diestrus, amphetamine decreased noradrenaline and increased normetanephrine concentrations, whereas at both proestrus and metoestrus the drug decreased noradrenaline but had no effect on normetanephrine concentrations. During the immediate post-ovulatory stage of the cycle, amphetamine altered the relative concentrations of catecholamines at the different stages of the estrous cycle. After amphetamine administration at estrus, catecholamine concentrations were similar to those seen at diestrus. The results suggest that the efficacy of amphetamine may be modified by fluctuations in hormone levels. 17 references. (Author abstract modified)

002106 Fontaine, J.; Reuse, J. Laboratory of Pharmacology, Free Unversity of Brussels, C.P. 205/7, Faculty of Medicine, B-1050 Brussels, Belgium **Pharmacological analysis of the effects of substituted benzamides on the isolated guinea-pig ileum. Study of metoclopramide, sulpiride, bromopride, tiapride and sultopride.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 235(1):51-61, 1978.

The effects of metoclopramide (Mcp), sulpiride (Sp), bromopride (Br), tiapride (Ti), and sultopride (Stp) on the isolated guinea-pig ileum were compared. Br, Ti, and Mcp had an indirect cholinergic stimulating effect on the intestinal smooth muscle, whereas Sp and Stp were devoid of this effect. At high doses, all the benzamides had a direct inhibitory effect on the ileum. Mcp, Br, and Ti (0.00001M) potentiated the responses of the ileum to acetylcholine (ACh). At high doses (0.0001M), the effects of all benzamides on responses to ACh or tohistamine were mostly inhibitory. Mcp and Br (0.00001M) inhibited the responses of the ileum to serotonin (5HT), while Ti, Sp, and Stp potentiated them. The potentiated responses to ACh and 5HT were abolished in the presence of tetrodotoxin or in the absence of calcium ions. 32 references. (Author abstract modified)

002107 Frankos, Vasilios Harry. University of Maryland **Characterization of norepinephrine metabolism following simultaneous intraventricular injection of H3L-tyrosine and C14DL-norepinephrine in rat brain. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 7800658, HC$15. MF$7.50. 112 p. 1977.

Simultaneous intraventricular injection of (2,6-H3)-L-Tyrosine and (7-C14)D,L Norepinephrine was used to characterize the metabolism of exongenously versus endogenously labeled brain norepinephrine (NE) in the rat brain. A new column chromatographic separation procedure was developed which allowed the simultaneous separation of the major catecholamine metabolites from a single rat brain. The results of the study demonstrate quite different metabolic profiles for endogenously synthesized NE and exogenously administered NE. By using desmethylimipramine, haloperidol, lithium and probenecid treatments, the study also demonstrated the comparability of using reuptake NE or endogenously synthesized NE for the study of drug effects

on brain NE metabolism. In all drug treatments differences and similarities in the metabolism of C14-NE and H3-NE were observed. The large differences in the metabolism of reuptake and newly synthesized NE raise many questions concerning the validity of using exogenous NE for the study of drug effects on the brain. (Journal abstract modified)

002108 Freed, William J.; Luchins, Daniel J.; Gillin, J. Christian; Wyatt, Richard Jed. Laboratory of Clinical Psychopharmacology, Intramural Research Program, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Wheat gluten impedes absorption of haloperidol.** Biological Psychiatry. 13(6):769-771, 1978.

The effects of wheat gluten on absorption of haloperidol were examined in adult female mice. Animals were deprived of food for 18 hours prior to administration of 2g/kg of wheat gluten or soy flour in distilled water by gastric intubation. After 20 minutes, mice were again intubated with 1mg/kg haloperidol. Mice were sacrificed at 20, 60, and 180 minutes after haloperidol. Results indicated that gluten significantly decreased the time course of both plasma and brain radioactivity 60 minutes after haloperidol administration, and also tended to produce decrease in plasma radioactivity after 180 minutes. Findings are most easily interpreted in terms of an interference by gluten with rate of haloperidol absorption from the gastrointestinal tract. Results are discussed in relationship to findings of Singh and Kay (1976) in schizophrenic patients. 5 references.

002109 French, Edward D.; Garcia, Joseph F.; George, Robert. Salk Institute, Center for Behavioral Neurobiology, La Jolla, CA 92037 **Acute and chronic morphine effects on plasma corticosteroids and growth hormone in the cat.** Psychoneuroendocrinology (Oxford). 3(3/4):237-244, 1978.

Evidence is presented that low doses of intravenous morphine in the cat causes an elevation of both corticosteroid and growth hormone in plasma. Corticosteroid levels did not continue to increase in concert with the dose of morphine, but the level of growth hormone did. Tolerance developed to the effects of morphine on corticosteroid, but not to the effect on growth hormone. Naloxone precipitated withdrawal was associated with an increase in plasma corticosteroid, but not growth hormone. 22 references. (Author abstract)

002110 Frenk, Hanan; Engel, Jerome, Jr.; Ackermann, Robert F.; Shavit, Yehuda; Liebeskind, John C. Department of Psychology, Tel-Aviv University, Ramat Aviv, Israel **Endogenous opioids may mediate post-ictal behavioral depression in amygdaloid-kindled rats.** Brain Research (Amsterdam). 167(2):435-440, 1979.

Naloxone reduced and morphine greatly enhanced the behavioral depression seen in Sprague-Dawley rats after generalized amygdaloid kindled seizures. Neither drug affected the threshold, intensity, or duration of any ictal manifestation of the seizure. These findings support the hypothesis that endogenous opioids are involved in certain seizure phenomena, but provide no evidence that opioid release underlies any of the initiating of regenerative neural processes responsible for the ictal phase of amygdaloid kindled seizures. Although these results indicate that opioids released during ictus play a role in the posticta depressive state, preliminary data from kindled rats and epileptic patients suggest that naloxone may exacerbate subsequent seizures. 16 references.

002111 Fujimura, Hajime; Tsurumi, Kaito; Nozaki, Masakatsu; Hori, Mikio; Imai, Eiji. Department of Pharmacology, Gifu University School of Medicine, Gifu 500, Japan **Analgesic activity and opiate receptor binding of 1-cyclohexyl-4-(1,2-diphenylethyl)piperazine.** Journal of Japanese Pharmacology (Kyoto). 28(3):505-506, 1978.

The relationship between the receptor binding and the analgesic activity of 1-cyclohexyl-4-(1,2-diphenylethyl)piperazine and its optical isomer R(-)-1,2-diphenyl-1-dimethylaminoethane was investigated. Analgesic activities were evaluated in mice by the tail pinch method. Inhibition of the electrically-induced contractions of the longitudinal muscle of the guinea pig ileum by the agonists applied cumulatively was also investigated. Results suggest that R(-)-enantiomer interacts with the opiate receptor in a mode similar to that seen with morphine, but the S()-isomer acts in a different mode and the racemate in a two way mode. Problems arising from the explanation of these results are described. 6 references.

002112 Fuller, Ray W.; Hemrick, Susan K. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Selective in vivo inhibition of monoamine oxidase in rat tissues by N (2-(o-chlorophenoxy) cyclopropylamine.** Proceedings of the Society for Experimental Biology and Medicine. 158(3):323-325, 1978.

The inhibition of monoamine oxidase (MAO) activity by N-(2-(o-chlorophenoxy)-ethyl)-cyclopropylamine hydrochloride (Lilly-51641) was examined in male Wistar rat tissues in vivo, using serotonin oxidation as an index of type-A MAO activity and phenylethylamine oxidation as an index of type-B MAO acitivity. Both at 1 and 24 hours, Lilly-51641 inhibited serotonin oxidation to a greater extent than phenylethylamine oxidation in brain, heart, and liver. After a 30mg/kg dose, Lilly-51641 produced a long-lasting inhibition of serotonin oxidation in all three tissues (half-life 3-6 days). In contrast, the initial half-life of inhibition of phenylethylamine oxidation was only 0.3-0.4days in brain and liver and 4 days in heart. These findings indicate that Lilly-51641 is a selective types-A MAO inhibitor and does not irreversibly inhibit type-B MAO in vivo. 10 references. (Author abstract modified)

002113 Fuller, Ray W.; Hemrick, Susan K.; Perry, Kenneth W. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Modification by harmaline of the effects of N-cyclopropyl-p-chloro-amphetamine on 5-hydroxyindole concentration in rat brain.** Journal of Pharmacy and Pharmacology (London). 31(1):53-54, 1979.

The effects of harmaline and N-cyclopropyl-p-chloroamphetamine (N-cyclopropyl-PCA) of 5-hydroxytryptamine (5-HT) concentrations in male Wistar rats brain were studied. The oxidation of 5-HT was inhibited by 75% and that of phenethylamine by 80% 24 hours after ip injection of N-cyclopropyl-PCA. Harmaline alone did not significantly inhibit either form of monoamine oxidase, but harmaline antagonized the inhibition of 5-HT oxidation by N-cyclopropyl-PCA. In brain homogenates from rats treated with both drugs, the oxidation of 5-HT was depressed only 20% below control level. The inhibition of phenetylamine oxidation by N-propyl-PCA was only slightly influenced by harmaline. N-cyclopropyl-PCA alone markedly reduced 5-hydroxyindoleacetic acid (5-HIAA) concentration, without affecting 5-HT concentration; harmaline alone did not alter the 5-HT concentration. In rats given harmaline and N-cyclopropyl-PCA, 5-HT was significantly depressed and 5-HIAA concentration was lowered to about the same extent as in rats treated with N-cyclopropyl-PCA alone. 8 references.

002114 Gallager, Dorothy W.; Thomas, John W.; Tallman, John F. Dept. of Psychiatry, Yale University School of Medicine, New Haven, CT 06508 **Effect of GABAergic drugs on benzodiazepine binding site sensitivity in rat cerebral cortex.** Biochemical Pharmacology (Oxford). 27(23):2745-2749, 1978.

The effects of gamma-aminobutyric acid (GABA) agonists on benzodiazepine binding site sensitivity in rat cerebral cortex

were examined. The pretreatment of rats in vivo with GABA agonists and drugs which increase GABA levels in brain led to an increased affinity of (3H)diazepam binding sites in rat cerebral cortex. These drugs included amino-oxyacetic acid, muscimol, gamma butyrolactone, and beta-(rho-chlorophenyl)-GABA; pentobarbital and thiosemicarbazide were without major effect. It is concluded that bicuculline and picrotoxin (at high concentrations) reverse this increase in (3H)diazepam binding site affinity. 38 references. (Author abstract modified)

002115 Galzigna, L.; Garbin, L.; Bianchi, M.; Marzotto, A. Institute of Biological Chemistry, CNR, I-35100 Padova, Italy **Properties of two derivatives of gamma-aminobutyric acid (GABA) capable of abolishing cardiazol- and bicuculline-induced convulsions in the rat.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 235(1):73-85, 1978.

The synthesis, chemical characteristics, biochemical properties, and anticonvulsant action of the N-benzoyl (BG1) and N-pivaloyl (PG2) derivatives of gamma-aminobutyric acid (GABA) are described. Unlike 14C-GABA, 14C-BG1 and 14C-PG2 were able to penetrate the blood/brain barrier in Wistar rats after subcutaneous injection. BG1 reached its highest concentration in brain 5 minutes after injection and PG2 after 30 minutes; this difference appeared to be related to the different hydrophobic character of the two compounds and to different diffusion rates. Pretreatment with BG1 or PG2 abolished convulsions induced in rats by pentetrazole or bicuculline. BG1 and PG2 had a slight inhibitory effect on glutamic acid decarboxylase, and both compounds acted as substrates for the action of proteolytic enzymes that convert the two compounds back go GABA. BG1 and PG2 were apparently nontoxic in doses up to 1g/kg. Glutamate oxidation by rat brain mitochondria was not affected by either compound. 8 references. (Author abstract modified)

002116 Gambhir, S. S.; Kapoor, N. K.; Das, P. K. Department of Pharmacology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India **Tissue catecholamines in Rana tigrina and effects of reserpine.** Japanese Journal of Pharmacology (Kyoto). 28(3):493-495, 1978.

The effects of reserpine on tissue catecholamine (CA) levels in adult frogs (Rana tigrina) of both sexes were studied. Tissues of the frogs were found to contain all three CAs, adrenaline (AD), dopamine (DA), and noradrenaline (NE). Total and individual CAs were significantly higher in the brain than in the heart. Reserpine treatment significantly, but only moderately, reduced DA levels in both the heart and brain and AD in brain only without affecting NE in either tissue. It is suggested that the relatively high DA content may represent a possible physiological role of this amine in this species, in additions to AD, which is the main transmitter in other related species. 11 references.

002117 Garcia-Sevilla, Jesus A.; Magnusson, Tor; Carlsson, Arvid; Leban, Johann; Folkers, Karl. Dept. of Pharmacology, University of Goteborg, Fack, S-40033 Goteborg, Sweden **Neurotensin and its amide analogue (Gln4)-neurotensin: effects on brain monoamine turnover.** Naunyn Schmiedeberg's Archives of Pharmacology (Berlin). 305(3):213-218, 1978.

The effects on brain monoamine turnover of neurotensin and its amide analogue, (Gln4)-neurotensin, were investigated. Intracerebroventricularly administered neurotensin and (Gln4)-neurotensin increased the formation of dopa in different brain regions of rats after inhibition of the aromatic L-amino acid decarboxylase. In the corpus striatum, (Gln4)-neurotensin was twice as active as neurotensin and it tended to be more active also in other brain regions. Brain tyrosine and 5-hydroxytryptophan concentrations were also increased. It is noted that both substances accelerated the disappearance of dopamine, noradrenaline, and 5-hydroxytryptamine after inhibition of monoamine synthesis. 32 references. (Author abstract modified)

002118 Gardier, Robert W.; Tsevdos, Estelle J.; Jackson, Daniel B.; Delaunois, August L. Ohio State University, Columbus, OH 43210 **Distinct muscarinic mediation of suspected dopaminergic activity in sympathetic ganglions.** Federation Proceedings. 37(10):2422-2428, 1978.

At the Annual Fall Meeting of the American Society for Pharmacology and Experimental Therapeutics held in Columbus, August 23, 1977, a paper was presented in which the enhancing effects of the competitive neuromuscular blocking agents, gallamine and pancuronium, on the nictitating membrane contraction in the cat were investigated. Inhibition of ganglionic muscarinic hyperpolarization, in response to short tetanic bouts of preganglionic cervical sympathetic stimulation, was found to be associated with enhanced contraction of the nictitating membrane. The action of gallamine and pancuronium conforms to a speculative cholinergic antagonism at the specific muscarinic receptors on the ganglionic dopaminergic interneuron. Effects of haloperidol and apomorphine are mentioned. Ganglionic slow depolarization mediated through the muscarinic receptors was found to be unaltered by any of the agents studied. 21 references. (Author abstract modified)

002119 Glennon, Richard A.; Liebowitz, Stephen M.; Mack, Elizabeth C. Dept. of Pharmaceutical Chemistry, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Serotonin receptor binding affinities of several hallucinogenic phenylalkylamine and N,N-dimethyltryptamine analogues.** Journal of Medicinal Chemistry. 21(8):822-825, 1978.

Using a rat stomach fundus model, the 5-hydroxytryptamine (5-HT) receptor binding affinities of several of the phenylalkylamine and N,N-dimethyltryptamine analogues were determined and compared. The most behaviorally potent analogues examined, DOB, DOM, and 5-methoxy-N, N-dimethyltryptamine, were found to possess rather high affinities for the 5-HT receptors of the model system. It is concluded that further investigations employing this model might help elucidate the binding phenomena involved in, and the structural requirements necessary for, this hallucinogen/5-HT receptor interaction. 32 references. (Author abstract modified)

002120 Goldberg, Leon I.; Kohli, Jai D.; Kotake, Alvin N.; Volkman, Paul H. Department of Pharmacological Sciences, University of Chicago, Chicago, IL 60637 **Characteristics of the vascular dopamine receptor: comparison with other receptors.** Federation Proceedings. 37(10):2396-2402, 1978.

At the Annual Fall Meeting of the American Society for Pharmacology and Experimental Therapeutics held in Columbus, August 23, 1977, a paper was presented in which structure-activity relationships of a series of flexible and semirigid agonists of the dopamine (DA) vascular receptor are described, and information concerning the relative efficacy of these agonists on other receptors in the cardiovascular system is presented. Injections of DA into the renal artery of phenoxybenzamine pretreated dogs produced vasodilation by action on a specific vascular receptor whose activation requirements are stringent. Phenylethylamine analogs found to be DA vascular agonists are listed. It is suggested that the preferred conformation for action of DA on vascular receptors is the beta rotameric trans form. Studies of agonists for other cardiovascular actions demonstrate that it is possible to produce analogs with different spectrums of activity than DA. From a comparison of the actions of agonists and antagonists of the DA vascular receptor and other DA receptor

models, it is concluded that either the vascular DA receptor is different than other DA receptors or other models are measuring phenomenons unrelated to DA receptors. 68 references. (Author abstract modified)

002121 Goldman, Patricia Shoer. Section on Developmental Neurobiology, Laboratory of Neuropsychology, NIMH, Bethesda, MD 20014 **Contralateral projections to the dorsal thalamus from frontal association cortex in the rhesus monkey.** Brain Research (Amsterdam). 166(1):166-171, 1979.

Following injection of a mixture of tritiated proline and leucine into three areas of the frontal lobe (middle of the dorsal bank of the principal sulcus, inferior prefrontal convexity, and medial orbital gyrus) of infant and juvenile rhesus monkeys, a distinct bilateral distribution of corticothalamic terminals was observed. As expected, heavy concentrations of label were found in the reticular, ventral anterior, and mediodorsal nuclei of the injected hemisphere. In addition to these established ipsilateral projections, however, considerable radioactivity was observed in thalamic areas in the opposite hemisphere. Contralateral projections from the cortex of the principal sulcus terminated primarily in the lateral parvocellular portion of the mediodorsal nucleus. Contralateral fibers from the orbital cortex projected to the magnocellular subdivision situated more medialy in the nucleus. The inferior convexity of the frontal lobe issued contralateral projections to cells lying intermediate to and overlapping the parvocellular and magnocellular moieties of the mediodorsal nucleus. The radioactive label appeared to reach the contralateral thalamus by a direct monosynaptic route from the injected area rather than by transneuronal transport. 21 references.

002122 Goldstein, Toby Reva. University of California, Los Angeles **Effect of acute and chronic administration of morphine on cholinergic mechanisms in the central nervous system.** Dissertation Abstracts International. 39(5):2244-B, 1978. Ann Arbor, Univ. Microfilms No. 7820223, 163p., 1978.

The effect of acute and chronic administration of morphine on cholinergic mechanisms in the CNS of rats and mice was investigated in three experiments. In Experiment 1 the dynamics of the cholinergic system were examined via acetylcholine (ACh) turnover studies. Results show that an acute administration of morphine decreased the turnover rate in mouse whole brain, and in rat hippocampus, cortex, and caudate. This reaction is reversed by naloxone. ACh turnover rates in the hippocampus were unchanged in the tolerant dependent state but decreased in whole mouse brain and cortex during withdrawal. Results suggest the presence of a cholinergic deficit during withdrawal. In Experiment 2, studies were undertaken to determine whether changes in high affinity uptake of choline into synaptosomes paralleled the direction of change in ACh turnover rates. Results suggest that either high affinity choline uptake is not the rate limiting step in ACh synthesis, or that morphine interferes with normal regulatory mechanisms of ACh synthesis. In Experiment 3, effects of acute and chronic administration of morphine on ACh transport in the brain were examined. A functional role for ACh uptake in the brain is not indicated. (Journal abstract modified)

002123 Goodrich, Cecilie; Choy, Marina. Department of Biology, Cleveland State University, Cleveland, OH 44115 **Body temperature and 5-hydroxytryptamine during early postnatal maturation in mice.** Developmental Psychobiology. 11(6):531-540, 1978.

The relationship between maturational increases in body temperature and brain indoleamines was explored through altering brain 5-hydroxytryptamine (5-HT) content. Effects on body temperature at approximately constant ambient temperature were studied following pharmacological manipulations in mice up to 16 days postpartum. Administration of 5-hydroxytryptophan to increase 5-HT levels was associated with decreased body temperature throughout the maturational period. Depletion of 5-HT with p-chlorophenylalanine was associated with increased body temperature at all ages studied, although 5-HT depletion was less effective in young animals than in older animals. The drug NSD-1034 acts at a different enzymatic step, and is effective in both central and peripheral tissues to reduce 5-HT and norepinephrine levels. NSD-1034 decreased body temperature up to 10 days of age, but the effect was reversed at about 14 days, and the drug increased body temperature significantly in 16-day-old animals. These results suggest a role for 5-HT in the mechanisms of heat production in early postnatal life. 27 references. (Author abstract modified)

002124 Green, Jack Peter; Johnson, Carl Lynn; Weinstein, Harel; Kang, Sungzong; Chou, David. Mount Sinai School of Medicine, City University of New York, New York, NY 10029 **Molecular determinants for interaction with the LSD receptor: biological studies and quantum chemical analysis.** In: Stillman, R., The psychopharmacology of hallucinogens. New York, Pergamon, 1978. 338 p. (p. 28-60).

A paper read at the workshop assessing hallucinogenic behavior sponsored by the Division of Research of the National Institute on Drug Abuse in Bethesda, Maryland, December 1976, is presented. Potencies of a series of tryptamines were measured in three different systems: contraction of the fundus of the rat stomach, inhibition of binding of D-lysergic acid diethylamide (D-LSD) by rat brain membranes, and inhibition of uptake of 5-hydroxytryptamine (5-HT) by rat synaptosomes. The potencies of stomach contractions correlated with those in inhibiting D-LSD binding by brain membranes. Results from molecular orbital calculations were used to define reactivity indices for tryptamines: electrostatic interaction potentials and maps of susceptibility to polarization. These indices show the importance of contour value 4-5 and the bridge regions in polarization complexes. From the electrostatic potential maps, force vectors were derived. Reactivity indices were tested; this supported the validity of using electrostatic interaction potentials as reactivity indices. The interaction of 5-HT as an electron donor with imidazolium as an electron acceptor was studied. The results support the use of force vectors as criteria for the orientation of reacting molecules in polarization complexes. The charge redistribution resulting from the 5-HT interaction with imidazolium showed that charge transduction occurs when a positive site on imidazolium interacts with the indole nitrogen. This transduction strengthens the complex and could help to explain the importance of nitrogen in activity. 92 references.

002125 Greenberg, Jeffrey H.; Mellors, Alan; McGowan, John C. Guelph-Waterloo Centre for Graduate Work in Chemistry, University of Guelph, Guelph, Ontario, N1G 2W1, Canada **Molar volume relationships and the specific inhibition of a synaptosomal enzyme by psychoactive cannabinoids.** Journal of Medicinal Chemistry. 21(12):1208-1212, 1978.

The ability of a number of lipophilic compounds to inhibit the mouse brain synaptosomal enzyme acyl coenzyme A:lysophosphatidylcholine acyltransferase was studied in vitro. Psychoactive cannabinoids inhibit the enzyme at concentrations much lower than was predicted from their capacity to act as lipid soluble anesthetics. Nonpsychoactive cannabinoids do not show specific inhibition. Molar volume relationships are used to show that, while all lipid soluble molecules exert some inhibitory effect in proportion to their ability to dissolve in biological membranes, psychoactive cannabinoids have an inhibitory effect greatly in excess of their anesthetic potency. The isoprenoid

convulsant thujone has been suggested to have psychoactivity similar to cannabinoids, but does not mimic the cannabinoids in inhibiting the synaptosomal enzyme. Molar volumes and specific interactions are used in structure activity correlations which yield information on the relative concentrations of biophase in drug responsive systems and the specificity of membrane active drugs. 32 references. (Author abstract)

002126 Greenfield, Susan A.; Chubb, I. W.; Smith, A. D. University Laboratory of Physiology, Oxford, England **The effect of chlorpromazine on the concentration of acetylcholinesterase in the cerebrospinal fluid of rabbits.** Neuropharmacology (Oxford). 18(2):127-132, 1979.

Intravenous administration of 4mg/kg chlorpromazine resulted in an increase (up to fivefold) in the concentration of acetylcholinesterase (AChE) in cerebrospinal fluid (CSF) sampled from the cisterna magna, but not in CSF from a lateral ventricle of New Zealand white male rabbits. The pattern of multiple molecular forms and specific activity of AChE in CSF did not resemble that of blood plasma, thereby excluding a breakdown of the blood/CSF barrier. A nonspecific increase in permeability of cell membranes seems unlikely, since the concentration of lactate dehydrogenase in cisternal CSF did not change. Prior administration of 3mg/kg iv atropine sulphate prevented the effect of chlorpromazine, but the same dose of atropine methylnitrate had no effect. The possibility that the rise in the concentration of AChE was the result of increased activity of central neurons containing this enzyme is discussed. 27 references. (Author abstract modified)

002127 Groppetti, A.; Parenti, M.; Cattabeni, F.; Maggi, A.; De Angelis, L.; Monduzzi, M.; Racagni, G. Institute of Pharmacology, University of Milan, Milan, Italy **Dopaminergic receptor activity in substantia nigra in the mechanisms of autoregulation of striatal dopamine release.** Advances in Biochemical Psychopharmacology. 19:363-371, 1978.

The role of nigral dopamine receptors in regulating the release of dopamine in the striatum is discussed. Neurochemical and pharmacological experiments in rats suggest that the activation of nigral dopamine adenylate cyclase by apomorphine and the blockade of the nigral receptors by haloperidol may be responsible for the changes in dopamine metabolism induced by these drugs, rather than postsynaptic feedback involving a gamma-aminobutyric acid containing pathway. The haloperidol-induced increase in dopamine metabolites in kainic acid lesioned rats and the antagonism of this effect by apomorphine indicate the existence of regulatory mechanisms that are independent of the integrity of neuronal impulse flow. 49 references.

002128 Grossman, Sebastian P.; Dacey, Dennis; Halaris, Angelos E.; Collier, Timothy; Routtenberg, Aryeh. Committee on Biopsychology, Department of Behavioral Sciences, University of Chicago, Chicago, IL 60637 **Aphagia and adipsia after preferential destruction of nerve cell bodies in hypothalamus.** Science. 202(4367):537-539, 1978.

The role which neurons, intrinsic to the lateral hypothalamus, play in the regulation of ingestive behavior was investigated. Microinjections of the excitatory neurotoxin kainic acid into the lateral hypothalamus of rats produced a period of aphagia and adipsia. Kainate treated rats displayed transient motor effects during the first hours after the injection, but did not show the persisting sensory motor and arousal disturbances typically observed in animals with electrolytic lesions in this part of the hypothalamus. Histological examination revealed a significant reduction in the number of nerve cell bodies in the lateral hypothalamus. Silver stained material indicated no evidence of damage to fiber systems passing through the affected region. Assays of dopamine in hypothalamus, striatum, and telencephalon did not indicate significant differences between experimental animals and controls. Results are in agreement with recent reports of the anatomical and biochemical effects of intracerebral kainic acid injections and suggest that the observed effect on feeding behavior is related to the destruction of neurons in the lateral hypothalamus. 28 references. (Author abstract modified)

002129 Guidotti, A.; Toffano, G.; Baraldi, M.; Schwartz, J. P.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **A molecular mechanism for the facilitation of GABA receptor function by benzodiazepines. (Unpublished paper).** Bethesda, MD, NIMH, 1978. 16 p.

Results obtained in support of the view that specific binding site for benzodiazepines can be associated with the regulation of GABAergic transmission are summarized. It is shown that high affinity binding of benzodiazepines and the regulation of Na independent high affinity binding of GABA depend on the interaction of benzodiazepines with an endogenous membrane constituent which functions as a modulator of high affinity GABA binding. It is reported that this is the first time that a specific protein part of a receptor has been isolated, purified, and characterized as a site for drug action. It is hypothesized that it is not expected that inhibitors of protein kinase modeled after the active site of the endogenous modulators may be pharmacological antagonists of benzodiazepines because although they may retain the capability of interacting with the endogenous inhibitor, the action will not be as specific as that of benzodiazepines. 15 references.

002130 Guyenet, Patrice G.; Aghajanian, George K. Dept. of Pharmacology, University of Virginia School of Medicine, Charlottesville, VA 22903 **ACh, substance P and met-enkephalin in the locus coeruleus: pharmacological evidence for independent sites of action.** European Journal of Pharmacology (Amsterdam). 53(4):319-328, 1979.

Cholinergic, opioid, and substance P receptors in the male Sprague-Dawley rat locus coeruleus (LC) were characterized, using microiontophoretic techniques. The muscarinic antagonist scopolamine blocked the response to acetylcholine (ACh) without modifying the excitation caused by glutamate or the inhibition caused by gamma-aminobutyric acid (GABA). Scopolamine did not modify the excitation of LC neurons induced by substance P or the inhibition induced by met-enkephalin. Naloxone antagonized the action of met-enkephalin, but did not alter the inhibition induced by GABA or the excitation induced by substance P. Baclofen antagonized the responses of LC neurons to all excitatory neurotransmitters. Results indicate that cholinergic transmission in the LC is purely muscarinic, and that substance P and met-enkephalin do not act in the LC by modulating the release of ACh or by interfering with its postsynaptic activity. Substance P had no apparent opioid agonist or antagonist activity. It is concluded that ACh, met-enkephalin, and substance P act upon pharmacologically distinct receptors in the LC. 40 references. (Author abstract modified)

002131 Haefely, W. E. Pharma Research Dept., Building 69, F. Hoffman-La Roche and Co. Ltd., CH-4002, Basel, Switzerland **Central actions of benzodiazepines: general introduction.** British Journal of Psychiatry (London). 133(September):231-238, 1978.

In a paper addressed to the April 7, 1978 Annual Meeting of the British Association for Psychopharmacology, evidence is presented which supports a specific facilitatory action of benzodiazepines on gamma-aminobutyric acid (GABA)-ergic synapses within the mammalian central nervous system. Benzodiazepines enhance presynaptic inhibition in the spinal cord and dorsal column nuclei as well as postsynaptic inhibition in dorsal

column nuclei, hippocampus, hypothalamus, cerebral cortex, cerebellar cortex, which are all examples of recurrent and collateral inhibition mediated by GABAergic intrinsic neurons. In addition, the compounds also enhance the inhibitory effect of GABAergic long projection neurons in the substantia nigra and the lateral vestibular nucleus of Deiters. Several problems remain to be solved, such as the exact site at which benzodiazepines initiate their action (presynaptically at GABAergic nerve endings or postsynaptically at the target cells) and the possible existence of endogenous ligands for the benzodiazepine receptor. Some suspected implications which studies on benzodiazepine binding sites could have for a deeper understanding of the mode of action of these drugs are discussed. 21 references. (Author abstract modified)

002132 Haglid, K. G.; Barclay, A. N.; Hamberger, A.; Hedquist, B.; Nystrom, B.; Sandberg, M. Institute of Neurobiology, University of Goteborg, Goteborg, Sweden **Comparison of rat brain membrane antigens by complement mediated release of neurotransmitters from brain fractions using antisera against S-100 and Thy-1.** Brain Research (Amsterdam). 168(1):119-132, 1979.

Synaptosomal, glial, and neuronal fractions were prepared from Sprague-Dawley rat brain, incubated with radioactively labeled neurotransmitters, and treated with antisera against S-100 and Thy-1. Treatment with the anti-(Thy-1) serum resulted in good release (50-75% of total uptake) of all neurotransmitters tested from synaptosomal and glial fractions. Gamma-aminobutyric acid (GABA) and glutamate, but not norepinephrine or serotonin, were released from neuronal perikarya. Anti-(S-100) serum gave no significant release of any neurotransmitter tested from any of the fractions, although all of them contain this protein. Results are compatible with the membrance nature of Thy-1 and the soluble nature of S-100 protein. Results with antiserum raised against bulk isolated rat neuronal perikarya suggest antigenic differences between neuronal and glial plasma membranes. 49 references. (Author abstract modified)

002133 Harden, T. Kendall; Mailman, Richard B.; Mueller, R. A.; Breese, George R. Department of Pharmacology, University of North Carolina, School of Medicine, Chapel Hill, NC 27514 **Noradrenergic hyperinnervation reduces the density of beta-adrenergic receptors in rat cerebellum.** Brain Research (Amsterdam). 166(1):194-198, 1979.

To assess the influence of noradrenergic hyperinnervation on beta-adrenergic receptor density, Sprague-Dawley rat pups were injected intracisternally with 6-hydroxydopamine (6-OHDA) within 24 hours of birth and sacrificed by decapitation at various times after treatment. Intracisternal injection of 10mcg 6-OHDA reduced the norepinephrine levels in the cerebral cortex by 90-99% and produced a 2.5-4.0fold increase in norepinephrine levels in the cerebellum; both these effects persisted until at least 110 days of age. The 6-OHDA treatment also induced a 50-72% increase in beta-receptor density in the cortex and a 20-30% increase in receptor density in the cerebellum. Thus, both hyperinnervation and hypoinnervation can affect the level of beta-adrenergic receptors. No alteration in the time course of receptor development or in the affinity of ligands for these receptors was observed. Results suggest that the extent of noradrenergic innervation may reciprocally influence the mechanisms by which postsynaptic cells respond to neurotransmitters. Under conditions of reduced innervation, a proliferation of beta-adrenergic receptors may occur to maintain the normal level of responsiveness of postsynaptic cells, while hyperinnervation may lead to a reduction in the number of receptor sites to prevent hyperresponsiveness of the noradrenergic system. 17 references.

002134 Harfenist, Morton; Soroko, Francis E.; McKenzie, Gerald M. Wellcome Research Laboratories, Research Triangle Park, NC 27709 **2-(Alkoxyaryl)-2-imidazoline monoamine oxidase inhibitors with antidepressant activity.** Journal of Medicinal Chemistry. 21(4):405-409, 1978.

The effects of a number of 2-imidazolines substituted in the 2 position by alkoxyaryl groups on mouse tapeworms, Hymenolepis nana and Oochoristica symmetrica were examined. Results were not highly successful against the primary cestode, but certain of the 2-(4-alkoxynaphthyl)-2-imidazolines and 2-(6-alkoxy-2-naphthyl)-2-imidzolines, however, had activity interpreted as antidepressant in the mouse. This activity paralleled in vitro irreversible inhibitory activity against mouse brain monoamine oxidase (MAO) for those where no substitution was present on the imidazoline ring. It is concluded that this irreversibility probably has a different origin from that postulated to explain the irreversible MAO inhibition of proparglic, cycloprophyl, and other chemically reactive MAO inhibitors. 20 references. (Author abstract modified)

002135 Harik, Sami I. Dept. of Neurology, P.O. Box 016960, Miami, FL 33101 **Effects of L-DOPA on putrescine levels in the brain and the liver of the rat.** European Journal of Pharmacology (Amsterdam). 54(3):235-242, 1979.

The effects of several amino acid precursors of putative neurotransmitters on putrescine levels in the brain and liver of male Sprague-Dawley rats were examined. L-DOPA increased brain and liver putrescine levels in a dose dependent manner, with maximum effect in 4-6 hours; the increase in liver putrescine was associated with a concomitant increase in ornithine decarboxylase activity. L-5-hydroxytryptophan increased liver putrescine, but had no effect on brain putrescine levels. D-DOPA and D-5-hydroxytryptophan were both ineffective in altering brain or liver putrescine. The effects of L-DOPA persisted after hypophysectomy and were not associated with changes in tissue levels of S-adenosylmethionine. Repeated administration of L-DOPA for periods of 48 and 96 hours resulted in a sustained elevation of putrescin thee levels in the brain but not in liver. 26 references. (Author abstract modified)

002136 Havemann, U.; Kuschinsky, K. Max-Planck-Institut fur experimentelle Medizin, Department of Biochemical Pharmacology, Hermann-Rein-Strasse 3, D-3400 Gottingen, Germany **Effects of opiates on cAMP in homogenates and slices of rat striata.** Pharmacology (Basel). 16(5):295-299, 1978.

In concentrations as low as 0.5mcM, morphine decreased the concentration of cyclic adenosine-3',5'-monophosphate (cAMP) in slices of male Wistar rat striata incubated in a depolarizing medium. This effect was inhibited by naloxone. Levorphanol, but not dextrorphan, induced an effect similar to that of morphine. In tissue homogenates, morphine (5-50mcM) also slightly decreased the concentration of cAMP; this effect was also antagonized by naloxone. No alterations in cAMP concentration were found in slices or homogenates from rats withdrawn from morphine. 17 references. (Author abstract modified)

002137 Hayes, Ronald L.; Price, Donald D.; Ruda, Maryann; Dubner, Ronald. Neurobiology and Anesthesiology Branch, National Institute of Dental Research, NIH, Bethesda, MD 20014 **Suppression of nociceptive responses in the primate by electrical stimulation of the brain or morphine administration: behavioral and electrophysiological comparisons.** Brain Research (Amsterdam). 167(2):417-421, 1979.

Electrical stimulation at various midbrain sites in rhesus monkeys suppressed the responses of certain classes of nociceptive spinothalamic tract neurons and reduced behavioral responses to noxious stimuli. Stimulation-induced suppression of spinothala-

mic neurons not antagonized by naloxone was indistinguishable from that produced by systemic morphine administration. Results are consistent with recent evidence suggesting the presence of mltiple supraspinal pathways projecting to the spinal cord which may mediate both narcotic and nonnarcotic modulation of nociceptive input within the dorsal horn. 16 references.

002138 Hazum, Eli; Chang, Kwen-Jen; Cuatrecasas, Pedro. Wellcome Research Laboratories, 3030 Cornwallis Road, Research Triangle Park, NC 27709 **Rapid degradation of (3H)leucine-enkephalin by intact neuroblastoma cells.** Life Sciences (Oxford). 24(2):137-144, 1979.

Enkephalin was rapidly degraded by N4TG1 neuroblastoma cells, which contain opiate receptors. The enzymatic activity was temperature dependent and was inhibited by bacitracin and puromycin. Digestion of intact cells with tryptsin greatly diminished the ability of the cells to degrade enkephalin, suggesting that the degradative enzyme is localized on the cell surface. Morphine, naloxone, leucine-enkephalin, methionine-enkephalin, and D-A1a2-substituted analogues at very high concentrations had no effect on enzymatic activity, even though they totally blocked binding of labeled enkephalin to receptors. Results suggest that there is no correlation between receptor occupancy and rate of enkephalin degradation. 21 references. (Author abstract modified)

002139 Heffner, Thomas G.; Seiden, Lewis S. Dept. of Pharmacological and Physiological Sciences, University of Chicago, 947 East 58th Street, Chicago, IL 60637 **The effect of depletion of brain dopamine by 6-hydroxydopamine on tolerance to the anorexic effect of d-amphetamine and fenfluramine in rats. (Unpublished paper).** Research Report, NIMH Grants MH-11191, MH-14247, MH-10562, 1978. 46 p.

The effects on food intake of repeated administration of d-amphetamine and fenfluramine were examined in rats adapted to a 4 hour per day feeding schedule. Control rats given daily injections of amphetamine prior to food access rapidly developed a partial tolerance to the food intake reducing effect of amphetamine. However, rats given a 6-hydroxydopamine treatment which produced a large selective depletion of dopamine in brain failed to display tolerance to amphetamine-induced anorexia after either 10 or 23 days of amphetamine injections. Although higher than normal doses of amphetamine were required to reduce feeding in 6-HDA treated rats, control rats displayed tolerance after repeated injections of drug doses which were either equianorexic or equivalent to doses used in rats given 6-HDA. Furthermore, 6-HDA treated rats failed to display tolerance to the low amphetamine normally used in control rats. In contrast to the results with amphetamine, both control and 6-HDA treated rats displayed tolerance to the anorexic effect of fenfluramine. These results suggest that central dopaminergic neurons are involved in the tolerance which normally develops to the anorexic effect of amphetamine. 64 references. (Author abstract modified)

002140 Hendler, Nelson H.; Livingston, Andrew. Osler 320, Johns Hopkins Hospital, Baltimore, MD 21205 **The localization over time of exogenous aldosterone and angiotensin II in various organs.** Pavlovian Journal of Biological Science. 13(3):187-193, 1978.

Radioactive aldosterone and angiotensin II were introduced via intracardiac injection in 18 rats to determine whether either of these substances naturally crosses the blood/brain barrier. Samples of blood, liver, kidney, adrenals, cerebral cortex, and hypothalamus were collected at 3, 15, and 60 minutes, frozen, dissolved, and counted. Blood levels for both chemicals remained constant over the study period. Aldosterone accumulated in liver, kidneys, adrenals, and hypothalamus 3 minutes after injection, and levels diminished over time. Angiotensin II levels peaked in the adrenal, kidney, and liver after 3 minutes, and in the hypothalamus after 15 minutes. Cerebral cortex levels were lower than hypothalamic levels by 30% for aldosterone and 50% for angiotensin II. Results suggest that both drugs may enter the central nervous system and selectively accumulate in the hypothalamus. 47 references. (Author abstract modified)

002141 Hertz, L.; Sastry, B. R. Dept. of Anatomy, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N 0W0 **Inhibition of gamma-aminobutyric acid uptake into astrocytes by pentobarbital.** Canadian Journal of Physiology and Pharmacology (Ottawa). 56(6):1083-1087, 1978.

Pentobarbital (0.5-2mM), but not phenobarbital, inhibited the uptake of gamma-aminobutyric acid (GABA) into mouse astrocytes in primary cultures by up to 45%. Excess potassium also inhibited GABA uptake in this system, and this effect was additive with that of pentobarbital. The importance of inhibition of GABA uptake for the pharmacological action of barbiturates is discussed. 41 references. (Author abstract modified)

002142 Hevor, T. K.; Gayet, J. Laboratoire de Physiologie Generale, Universite de Nancy I, Nancy, France **Fructose-1,6-biphosphatase and phosphofructokinase activities in the brain of mice submitted to methionine sulfoximine.** Brain Research (Amsterdam). 150(1):210-215, 1978.

The effect of methionine sulfoximine (MSO) administered to male Swiss mice on the activity of fructose-1,6-biphosphatase (FDPase) and phosphofructokinase (PFK) was investigated to show whether the cerebral accumulation of glucose and glycogen, induced by the convulsant, originates from an activation of gluconeogenesis. It was found that MSO administered to the mouse induces in the brain an increase in activity of the key gluconeogenic enzyme FDPase, during the preconvulsive and the convulsive periods, and also when the animals appeared normal. In the same experimental conditions, the activity of the key glycolytic enzyme PFK does not change significantly. It is concluded that the ultrastructural damages occurring in the mouse brain following administration of MSO do enhance gluconeogenesis, probably in astrocytes, through an activation and/or a de novo biosynthesis of FDPase. 16 references.

002143 Hicks, T. P.; Hall, J. G.; McLennan, H. Dept. of Physiology, University of British Columbia, Vancouver, BC, Canada V6T 1W5 **Ranking of excitatory amino acids by the antagonists glutamic acid diethylester and D-alpha-aminoadipic acid.** Canadian Journal of Physiology and Pharmacology (Ottawa). 56(6):901-907, 1978.

The effects of the antagonists D-alpha-aminoadipic acid (DaAA) and L-glutamic acid diethylester (GDEE) on the excitatory actions of amino acids on thalamic neurons of rats anesthetized with urethane were examined. The excitatory compounds could be ranked in their order of susceptibility to the two antagonists. Amino acids that were most susceptible to one antagonist were the least affected by the other antagonist; kainate was an exception, in that its actions were not effectively blocked by either antagonist. Results suggest that two populations of receptors exist, one at which GDEE preferentially blocks the actions of isomers of glutamate and aspartate, and the other at which DaAA is selective toward the more powerful excitants N-methyl-DL-aspartic acid, DL-homocysteic acid, and ()-cis-1-amino-1,3-dicarboxycyclopentane. The anomalous behavior of kainate suggests the existence of a third receptor type for this compound. 31 references. (Author abstract modified)

002144 Hirsch, Madelyn J.; Wurtman, Richard J. Department of Nutrition and Food Science, Massachusetts Institute of Tech-

nology, Cambridge, MA 02139 **Lecithin consumption increases acetylcholine concentrations in rat brain and adrenal gland.** Science. 202(4364):223-225, 1978.

The effects of choline administered as lecithin on serum and tissue choline and acetylcholine (ACh) concentrations in the rat were investigated. Consumption of a single meal containing lecithin, the major source of choline occurring naturally in the diet, increased the concentration of choline and ACh in rat brain and adrenal gland. Hence, the concentration of ACh in the tissues may normally be under direct, short-term nutritional control. 22 references. (Author abstract modified)

002145 Hitzemann, R. J.; Loh, H. H. Department of Psychology, University of California, San Francisco, CA 94143 **The measurement of phospholipids transport and turnover in the nigroneostriatal system using (3H)glycerol, (3H)choline and (32P)phosphoric acid. (Unpublished paper).** Research Report, NIMH Grant MH-25487, 1978. 1 p.

Male Sprague-Dawley rats were stereotaxically injected with 20uCi of (3H)glycerol or (3H)choline and 100uCi of (32P)phosphoric acid into the substantia nigra in a measurement of phospholipids transport and turnover in the nigroneostriatal system. The (3H)glycerol phospholipidss were rapidly transported to the neostriatum with the peak of radioactivity occurring prior to 24 hours after injection. Beginning on day 1, the (3H)glycerol phospholipidss showed a biphasic decline. The rapid component turnover accounted for the loss of 70% to 80% of the label in all four lipids measured. Alkaline methanolysis revealed that more than 85% of the label in the rapid component of transport and turnover was in the glycerol moiety. The slower component had a turnover of more than 14 days. It was concluded that the rapid phase of (3H)glycerol phospholipids turnover may be useful for studying the relationships between membrane turnover and drug action in the nigrostriatal system. (Author abstract modified)

002146 Hofmann, M.; Tonon, G. C.; Spano, P. F.; Trabucchi, M. Department of Pharmacology and Pharmacognosy, University of Milan, Via A. Del Sarto 21, 20129, Milan, Italy **Mechanisms of dihydroergotoxine's effect on prolactin release.** Journal of Pharmacy and Pharmacology (London). 31(1):42-44, 1979.

The effects of low doses of dihydroergotoxine (DHA) on prolactin secretion and striatal dopamine turnover were studied in male Sprague-Dawley rats. Serum prolactin concentrations were significantly decreased by 10mcg/kg intraventricularly administered DHE and were maximally inhibited by 40mcg/mcg. The decrease in prolactin concentration lasted for 6-8 hours. Intraperitoneal administration of 2.5mg/kg DHE decreased striatal dihydroxyphenylacetic acid (DOPAC) concentrations, but a lower dose was ineffective. Intraventricular injection of DHE induced a dose dependent decrease in DOPAC and homovanillic acid concentrations; this effect was apparent at a dose of 5-10mcg/kg and lasted for 5-6 hours. Results indicate that DHE acts at least partially through the dopaminergic system in the CNS. 29 references.

002147 Hofmann, M.; Jommi, G. C.; Montefusco, O.; Tonon, G. C.; Spano, P. F.; Trabucchi, M. Department of Pharmacology and Pharmacognosy, University of Milan, I-20129 Milan, Italy **Stereospecific effects of (-)sulpiride on brain dopamine metabolism and prolactin release.** Journal of Neurochemistry (Oxford). 32(5):1547-1550, 1979.

Sulpiride, an unusual neuroleptic, was resolved into its two enantiomers by a newly developed procedure. (-)Sulpiride was several times more potent than ()sulpiride in increasing male Sprague-Dawley rat prolactin secretion and 3,4-dihydroxyphenylacetate concentrations in striatum and limbic areas. These results are in agreement with clinical data showing that (-)sulpiride is the active form of the drug. 19 references. (Author abstract modified)

002148 Holl, J. E.; Resurreccion, V. A.; Park, L. E.; Caster, W. O. Dept. of Pharmacology, School of Pharmacy, University of Georgia, Athens, GA 30602 **Barbiturate and amphetamine activity in rats fed a magnesium-deficient diet.** Research Communications in Chemical Pathology and PhARMACOLOGY. 22(3):501-512, 1978.

Hexobarbital hypnosis and d-amphetamine toxicity were observed in rats fed a commercially available rat food preparation (lab chow) and in another two groups fed complete nutritionally defined diets with or without magnesium. Neither hexobarbital sleeping time nor hexobarbital blood concentration at awakening were affected after 4, 8, or 12 days of feeding the deficient diet. However, increased sensitivity to d-amphetamine was observed after 11 days of feeding the same magnesium deficient diet to other rats. The LD50 of d-amphetamine in magnesium deficient rats was less than 0.5that recorded for the groups fed lab chow or the nutritionally defined diet with a magnesium supplement. 23 references. (Author abstract)

002149 Holmgren, Bjorn; Urba-Holmgren, Ruth. Centro Nacional de Investigaciones Cientificas, Apartado 6990, Havana, Cuba **Ontogeny of two cholinergically mediated central effects: stereotyped yawning and potentiation of head-shaking.** Acta Neurobiologiae Experimentalis (Warszawa). 38(1):11-23, 1978.

The ontogenetic course of two cholinergically mediated central neuropharmacological effects, yawning and potentiation of head shaking induced by D-amphetamine (5mg/kg), was explored in developing rats. Physostigmine (0.1mg/kg) and pilocarpine (4mg/kg) evoked stereotyped yawning in neonatal rats, the effect declining in the middle of the second week of life. Both cholinomimetic drugs strongly potentiated amphetamine-induced head shaking between the fourth and tenth postnatal days. Pilocarpine was capable of inducing head shaking in the absence of amphetamine in rats from 8-12-days-old. Infant rat yawning and head shaking were blocked by scopolamine (5mg/kg). Nicotine (0.1mg/kg) potentiated head shaking but inhibited yawning. Yawning was also depressed by D-amphetamine. The early maturation of these cholinergic effects is discussed in comparison to the later maturation of several forebrain cholinergic systems. 38 references. (Author abstract)

002150 Honegger, Paul; Richelson, Elliott. Institut de Physiologie, Faculte de medecine, Universite de Lausanne, Switzerland **Neurotransmitter synthesis, storage and release by aggregating cell cultures of rat brain.** Brain Research (Amsterdam). 162(1):89-101, 1979.

Rotation mediated aggregating cell cultures of mechanically dissociated fetal (15-16 days gestation) Sprague-Dawley rat brains between 25 and 35 days in vitro were examined for their ability to synthesize neurotransmitters and putative neurotransmitters from radioactively labeled precursors added to the culture medium. Cultures derived from whole brain synthesized (3H)acetylcholine from (3H)choline, (3H)gamma-aminobutyric acid from L-(3H)glutamic acid, (3H)dopamine from L-(3H)tyrosine, (3H)dopamine and (3H)norepinephrine from L-(3H)dihydroxyphenylalanine, and (3H)serotonin from L-(3H)tryptophan. Veratridine increased and tetrodotoxin decreased the rate of (3H)dopamine synthesized by aggregates derived from midbrain and hindbrain. Reserpine markedly depleted (3H)dopamine from the aggregates. In chase experiments, veratridine significantly decreased the amounts of radioactivity labeled acetylcholine, L-glutamic acid, dopamine, and serotonin recovered from aggregates, whereas tetrodotoxin significantly

increased the amounts of labeled acetylcholine and dopamine recovered from the aggregates. Results indicate that the cultured cells synthesized neurotransmitters and suggest that some of these compounds were stored by and released from electrically active cells within the aggregates. 22 references. (Author abstract modified)

002151 Horn, A. S.; Grol, C. J.; Dijkstra, D.; Mulder, A. H. Department of pharmacy, University of Groningen, Groningen, The Netherlands **Facile syntheses of potent dopaminergic agonists and their effects on neurotransmitter release.** Journal of Medicinal Chemistry. 21(8):825-828, 1978.

The effects of potent dopaminergic agonists on neurotransmitter release were examined in vitro using rat brain slices. The facile syntheses of important intermediates used in the preparation of the two dopaminergic agonists, 2-amino-6,7-dihydroxytetrahydronaphthalene (ADTN) and its 5,6-dihydroxyl isomer are described. Thus 6, 7-dimethoxy-2-tetralone has been prepared in two steps and 5, 6-dimethoxy-2-tetralone in three steps, both from commercially available materials. It has been shown that both compounds, at a concentration of 2 mcM, cause a release of (3H)-DA and NA. ATN was found to be inactive in these experiments, which shows the improtance of the catechol function in this uptake/release process. 22 references. (Author abstract modified)

002152 Horng, Jong S.; Wong, David T. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Gamma-aminobutyric acid receptors in cerebellar membranes of rat brain after treatment with Triton X-100.** Journal of Neurochemistry (Oxford). 32(5):1379-1386, 1979.

Treatment of cerebellar membranes of male Sprague-Dawley rat brain with a low concentration of Triton X-100, followed by extensive washing, resulted in an increase in the sodium (Na) independent binding of tritiated gamma-aminobutyric acid (3H-GABA) and a total loss of the Na dependent binding of 3H-GABA. The Na independent binding of 3H-GABA was more abundant in membranes of cerbellum than of other brain regions and was localized primarily in the synaptic membrane fraction. In Triton treated membranes, the Na independent binding of 3H-GABA was a saturable process, which could be resolved into high and low affinity components with dissociation constants of 4.5and 30nM, respectively. Muscimol, GABA, imidazole acetic acid, and bicuculline inhibited the high affinity Na independent binding of 3H-GABA by 50% at 0.0003, 0.012, 0.3, and 10mcM, respectively. Results suggest that the Na independent binding of 3H-GABA in the Triton treated cerebellar membranes represents synaptic GABA receptors. 16 references. (Author abstract modified)

002153 Horodnicki, J. M.; Wasik, A.; Firko, M.; Janicka, B. Klinika Psychiatrii PAM, ul. Broniewskiego 32, Szczecin, Poland **/An experimental study of the influence of fluphenazine on the activity of key enzymes of brain glucose and leukocyte metabolism in rats./** Badania doswiadczalne wplywu flufenazyny na aktywnosc kluczowych enzymow przemiany glukozy mozgu i leukocytow u szczurow. Psychiatria Polska (Warszawa). 12(5-6):545-548, 1978.

An experimental study of the influence of fluphenazine on the activity of the key enzymes of brain glucose and leukocyte metabolism in rats is presented. Fluphenazine administered in 7mg doses per kg of body weight into the stomach of rats of the Wistar strain for 24 hours over 16 to 18 days caused a statistically significant raise in PFK, ALD and GAPDH activity in the brain and in ALD activity in leukocytes. The effect of fluphenazine on the activity of glucose enzymes is similar to the effect of imipramine rather than to that of chloropromazine. 8 references. (Journal abstract modified)

002154 Hoss, Wayne; Okumura, Kuniko; Formaniak, Michele; Tanaka, Ryo. Center for Brain Research, University of Rochester School of Medicine and Dentistry, Rochester, NY 14642 **Relation of cation binding sites on synaptic vesicles to opiate action.** Life Sciences (Oxford). 24(11):1003-1009, 1979.

The protein sensitized fluorescence of terbium ions (Tb3) was used to characterize cation binding sites on albino rat brain synaptic vesicles. In the presence of 100mM potassium chloride, the vesicles displayed a single class of sites with affinities for calcium and magnesium ions in the mM range. Morphine, which depletes calcium from nerve terminals in vivo, did not compete in vitro for the sites monitored by Tb3 fluorescence. Acute morphine treatment did not alter the binding of Tb to the synaptic vesicle fraction. It is suggested that the morphine-induced depletion of brain calcium is not mediated by a direct action of opiates on these membrane sites. 21 references. (Author abstract modified)

002155 Jacoby, J. H.; Poulakos, J. J.; Bryce, G. F. Department of Pharmacology, New Jersey Medical School, 100 Bergen Street, Newark, NJ 07103 **On the central anti-serotoninergic actions of cyproheptadine and methysergide.** Neuropharmacology (Oxford). 17(4/5):299-306, 1978.

The peripheral administration of cyproheptadine and methysergide to male Sprague-Dawley rats did not result in any changes in brain 5-hydroxyindole levels up to 2 hours after administration, but higher doses of cyproheptadine did produce a rise in brain tryptophan. Exposure to elevated ambient temperatures resulted in a similar rise in brain 5-hydroxyindoles in saline and cyproheptadine treated rats. Methysergide blocked the rise of 5-hydroxyindoleactic acid (5HIAA) following exposure to heat. Neither cyproheptadine nor methysergide prevented the decrease in brain 5HIAA levels following injection of quipazine. Results suggest that cyproheptadine and methysergide do not act as central serotonin receptor antagonists, or that they act upon serotonin receptors which do not mediate compensatory feedback responses. 56 references. (Author abstract modified)

002156 Jamali, F.; Axelson, J. E. Faculty of Pharmacy, University of Tehran, Tehran 14, Iran **Griseofulvin-phenobarbital interaction: a formulation-dependent phenomenon.** Journal of Pharmaceutical Sciences. 67(4):466-470, 1978.

The interaction of griseofulvin with phenobarbital was studied in male Wistar rats following oral administration of different dosage forms. A single dose of 15mg/kg phenobarbital 24 hours prior to the oral administration of a suspension of 100mg/kg griseofulvin in 0.5% polysorbate 80 significantly reduced plasma griseofulvin levels. An increase in the concentration of polysorbate 80 to 2% reduced the extent of the interaction from 50% to 32%. Phenobarbital did not influence plasma griseofulvin levels when griseofulvin was given in either 70% polyethylene glycol 300 or 100% polyethylene glycol 600. It is concluded that the drug interaction is formulation dependent and is a result of diminished dissolution and reduced absorption of griseofulvin. 19 references. (Author abstract)

002157 James, David T. D. Dept. of Psychology, New University of Ulster, Coleraine, Northern Ireland **Drug effects on spontaneous and septially-elicited hippcamal theta.** Irish Journal of Medical Science (Dublin). 147(Supplement 1):33-37, 1978.

A paper read at the first Irish Psychopharmacology Conference, held in Belfast in March 1978, is presented. Hypotheses concerning drug effects on the behavioral significance and neural control of the hippocamal theta rhythm are discussed.

The effects of sodium amylobarbitone and d-amphetamine sulphate upon spontaneously occuring hippocampal theta, and on theta elicited by electrical stimulation of the septum, were investigated in the freely moving rat. Conclusions differed according to the method employed. It is suggested that elucidation of the relationship between spontaneous and driven theta may help to reconcile the various bodies of data. 14 references. (Author abstract modified)

002158 Jori, Armanda; Caccia, Silvio; De Ponte, Piero. Istituto di Richerche Farmacologische 'Mario Negri,' Via Eritrea, 62 I-20157, Milan, Italy **Differences in the availability of d- and l-enantiomers after administration of racemic amphetamine to rats.** Xenobiotica (London). 8(10):589-595, 1978.

Following i.p. administration of racemic amphetamine to rats, the concentration of the d-enantiomer was significantly greater than that of the l-enantiomer in brain and plasma, but not in urine. When the two isomers were given separately, their brain concentrations were similar. The brain concentrations of d-amphetamine and l-amphetamine were also similar after i.p. administration of racemic amphetamine to mice or to rats pretreated with SKF525-A, an inhibitor of amphetamine hydroxylation. The possibility that the l-isomer can interfere with the hydroxylation of d-amphetamine is discussed. 23 references. (Author abstract modified)

002159 Joy, R. M.; Wong, D. L. Department of Physiological Sciences, University of California, School of Veterinary Medicine, Davis, CA 95616 **Evoked and spontaneous corticofugal multiple unit activity during different phases of metrazol infusion in cats.** Neuropharmacology (Oxford). 17(4/5):281-293, 1978.

Multiple unit activity (MUA) was recorded from the cerebral peduncle during preictal, ictal, and postictal phases of Metrazol activity increased; sustained MUA discharge preceded the onset of tonic EEG infusion in cats. During preictal EEG paroxysmal activity, MUA seizure activity, and bursts of MUA activity coincided with positive transients during later tonic and clonic periods. No MUA discharge was observed during postictal depression. During preictal periods, Metrazol increased the amplitude and duration of the initial MUA burst to stimulation of the ventralis posterolateralis nucleus. The duration and intensity of the MUA suppression following the response was also increased. The burst/suppression pattern of MUA activity during repetitive stimulation was replaced by a burst/sustained discharge pattern. Correlation of the changes observed in EEG and MUA with previously described intracellular changes indicates that axonal activity provides a more relevant indication of effective corticofugal activity than does intracellular recording. The level of axonal discharge correlates better with the degree of soma/dendritic depolarization than with somatic spike generation. 37 references. (Author abstract modified)

002160 Jung, M. J.; Palfreyman, M. G.; Wagner, J.; Bey, P.; Ribereau-Gayon, G.; Zraika, M.; Koch-Weser, J. Centre de Recherche Merrell International, 16 rue d'Ankara, F-67084 Strasbourg-Cedex, France **Inhibition of monoamine synthesis by irreversible blockade of aromatic aminoacid decarboxylase with alpha-monofluoromethyldopa.** Life Sciences (Oxford). 24(11):1037-1042, 1979.

Single doses (0.25-25mg/kg ip) of DL-alpha-monofluoromethyldopa (MFMD) caused partial to total inhibition of aromatic aminoacid decarboxylase (AADC) in male CD mouse kidney and heart. Inhibition of brain AADC was significant at MFMD doses above 2.5mg/kg and was complete at 100mg/kg. Enzyme activity began to return after 24 hours, so that repetition of a dose at 12 hour intervals markedly increased the inhibition. Single doses of 100-250mg/kg almost completely depleted kidney, heart, and brain of endogenous catecholamines by blocking dopa decarboxylation. Serotonin was also decreased, presumably by the same mechanism. 14 references. (Author abstract modified)

002161 Kalix, Peter. Departement de Pharmacologie, Ecole de Medecine, CH-1211 Geneva 4, Switzerland **Prostaglandins cause cyclic AMP accumulation in peripheral nerve.** Brain Research (Amsterdam). 162(1):159-163, 1979.

The effects of prostaglandins on cyclic adenosine monophosphate (AMP) levels in peripheral nervous tissue were examined. Incubation of sections of desheathed rabbit vagus nerve with E-type prostaglandins lead to accumulation of cyclic AMP, whereas incubation with F-type prostaglandins did not. Experiments with A-type and B-type prostaglandins showed that A1 and B2 had small but significant effects on cyclic AMP accumulation and that A2 and B1 had no effect. Results indicate that in peripheral nerves, as in the CNS, it is prostaglandins of the E-type that specifically affect cyclic AMP levels. 22 references.

002162 Kantak, K. M.; Wayner, M. J.; Stein, J. M.; Tilson, H. A. Laboratory of Behavioral Neurochemistry, Waisman Center -- Room 609, University of Wisconsin, 1500 Highland Avenue, Madison, WI 53706 **Effect of imipramine on serotonin turnover in the lateral hypothalamus.** Pharmacology Biochemistry and Behavior. 9(5):693-696, 1978.

The effect of imipramine on serotonin (5-HT) turnover in the lateral hypothalamus was investigated in six male hooded rats. One hour following an infusion of 3H-5-HT, animals were injected with either 15mg/kg imipramine hydrochloride or 0.9% NaCl and then the lateral hypothalamus was perfused for 40 min. Samples of perfusate were analyzed by thin layer chromatography for estimation of 3H labelled 5-HT and metabolites. Results indicate that imipramine hydrochloride 15mg/kg decreases serotonin release and turnover in the lateral hypothalamus. 17 references. (Author abstract modified)

002163 Kapitulnik, J.; Feuerstein, G.; Govrin, H.; Lichtenberg, D. Hebrew University-Hadassah Medical School, Jerusalem, Israel **Induction of drug-metabolizing enzymes by lithium in rat liver.** Israel Journal of Medical Sciences (Jerusalem). 14(9):997, 1978.

A summary of a paper read at the 41st Meeting of the Israel Physiological and Pharmacological Society held March 1978 in Jerusalem, is presented. The effect of lithium chloride (LiCL) administration to adult female rats on three representative drug metabolizing enzyme systems, using the postmitochondrial fraction of liver was investigated. After 12 days of treatment: 1) a 50% increase in benzo(a)-pyrene hydroxylase activity; 2) a two-fold increase in antipyrine hydroxylation; and 3) no change in 4-methylumbelliferone-UDPGA transferase activity, with or without digitonin were observed. After 21 days of treatment there was no differences in enzyme activities between lithium treated and control rats. However, increased activities were observed on day 22, after increasing the does of LiCl by 50% from day 13. Water intake which increased considerably during the first week of treatment but decreased later toward control values, could be stimulated again by increasing the dose of LiCL. Results suggest that lithium induces cytochrome P-450 dependent monooxygenases in rat liver, and that tolerance to this effect develops on chronic treatment, probably through increased elimination of lithium from liver cells. (Author abstract modified)

002164 Karlen, B.; Lundgren, G.; Miyata, T.; Lundin, J.; Holmstedt, B. Karolinska Institutet, Fack, S-104 01, Stockholm, Sweden **Effect of atropine on acetylcholine metabolism in the mouse brain.** In: Jenden, D., Cholinergic mechanisms and psy-

chopharmacology. New York, Plenum, 1978. 885 p. Vol. 24. (p. 643-655).

At the third Symposium on Cholinergic Mechanisms and Psychopharmacology, held in La Jolla, CA, March 1977, a paper evaluating the acute effect of atropine on the turnover rate of acetylcholine (TRACh) by studying incorporation during steady-state conditions and during the onset of the atropine effect was presented. Swiss albino male mice were injected with atropine sulfate and killed by microwave irradiation of the head at 15 seconds to 20 minutes thereafter. Results indicate that the effect of atropine on the endogenous level of ACh was very rapid; when atropine was given i.v. the levels in whole brain were decreased by 30% after 2 min. The effect on endogenous Ch was much less marked, but a small increase could be noted. Calculations for TRACh show no difference between controls and atropine treated animals in the whole brain, but in the striatum there was a small reduction after 25mg/0.1kg atropine sulfate. It is suggested that the decreased level of ACh after atropine injection is probably due to an increased release of the transmitter, since the turnover rate seems unaffected or at least not decreased 11 references.

002165 Kasuya, Y.; Suzuki, N. Dept. of Chemical Pharmacology, University of Tokyo, Tokyo 113, Japan **Regional differences in the effects of denervation, cocaine and chronic reserpine administration on the responses of the rat vas deferens to norepinephrine and acetylcholine.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 236(2):202-213, 1978.

The effects of denervation, cocaine, and chronic administration of reserpine on the responses of rat vas deferens to norepinephrine and acetylcholine were examined in the prostatic and epididymal halves. The epididymal half was found to be more sensitive to both drugs than the prostatic half and to have a more maximal response to norepinephrine. Denervation, cocaine, and chronic reserpine administration all produced supersensitivity to both drugs in the epididymal half; in the prostatic half supersensitivity to only norepinephrine was observed while responses to acetylcholine were somewhat suppressed. The effects of the three procedures on degree of supersensitivity and maximal response to the drugs in each half are presented. The results are discussed in relation to those previously obtained using whole vas deferens. 17 references. (Author abstract modified)

002166 Kataoka, Kiyoshi; Danbara, Hiroshi; Sunayashiki, Kosaku; Okuno, Sachiko; Sorimachi, Masaru; Tanaka, Michiyasu; Chikamori, Kazumasa. Department of Physiology, Ehime University, School of Medicine, Onsen-gun, Ehime, 791-02, Japan **Regional and subcellular distribution of gold in brain of gold thioglucose obese mouse.** Brain Research Bulletin. 3(3):257-263, 1978.

By employing neutron activation analysis, endogenous content of gold was estimated quantitatively in discrete brain areas and in subcellular fractions of the hypothalamus of gold thioglucose (GTG) induced obese mice. The highest concentration of gold was obtained in the ventromedial hypothalamus (VMH), reaching approximately 100ng/mg wet tissue. Significantly higher concentrations were observed in other hypothalamic subareas, followed by certain limbic areas and the thalamus, while in the cerebral and the cerebellar cortex the gold concentration was very low. Subcellularly, the hypothalamic gold was principally recovered in the supernatant fraction, particularly after a hyposmotic shock treatment of the crude mitochondrial fraction. Contrary to GTG, treatment with gold thiomalate (GTM) did not induce obesity in the mouse, although a considerable amount of gold was observed in the VMH, suggesting the existence in the VMH of at least a two step mechanism for inducing GTG obesity. To identify the satiety neuron transmitter, an analysis of certain enzyme activities involved in the synthesis of known transmitters, such as acetylcholine or gamma-aminobutyric acid (GABA) was made in the GTG obese mice. There were no significant changes in any of the areas functionally related to the VMH. 30 references. (Author abstract)

002167 Kato, G.; Carson, S.; Kemel, M. L.; Glowinski, J.; Giorgueieff, M. F. Laboratoire de Neurobiologie, ENS, 46 rue d'Ulm, Paris 5e, France **Changes in striatal specific 3H-atropine binding after unilateral 6-hydroxydopamine lesions of nigrostriatal dopaminergic neurones.** Life Sciences. 22(18):1607-1614, 1978.

Specific binding of 3H-atropine to crude synaptosomal membrane fractions of the rat striatum was measured at different times after unilateral 6-hydroxydopamine lesions of the nigrostriatal dopaminergic neurones. In a group of rats killed between 4 to 15 days after lesioning the right side, specific 3H-atropine binding was reduced by 20% compared to the right side of unlesioned rats. There was at concomitant increase (20%) of specific 3H-atropine binding in the contralateral side compared to control animals. Changes in muscarinic receptor binding depended on the time after which the lesions were made: maximum effects occurred about 8 days after lesioning but almost completely disappeared 13 days later. Dissociation constants for 3H-atropine in the right and left striata of control and lesioned rats were not significantly different. It is suggested that the decrease in muscarinic receptor binding in the ipsilateral striatum of lesioned animals may result from an activation of cholinergic neurones produced by removal of the inhibitory dopaminergic terminals. 19 references. (Author abstract modified)

002168 Kehr, Wolfgang; Speckenbach, Wolfgang. Dept. Neuropsychompharmakologie, Schering AG, Mullerstrasse 170-178, D-1000 Berlin 65 Germany **Effect of lisuride and LSD on monoamine synthesis after axotomy or reserpine treatment in rat brain.** Naunyn-Schmiedeberg's Archives of Pharmacology. 301(3):163-169, 1978.

The effect of lisuride and LSD on monoamine synthesis after axotomy or reserpine treatment in rat brain regions was evaluated using an in vivo method which the accumulation of dopa and 5-hydroxytryptophan was measured after inhibition of the aromatic amino acid decarboxylase by means of 3-hydroxybenzylhydrazine. LSD (50-1000mg/kg, i.p.)caused a dose dependent increase in dopa formation and slight elevation of tyrosine and tryptophan concentrations in the intact rat brain; moreover, it reduced the accumulation of 5-hydroxytryptophan. The increase in dopa formation in the terminal system of the rat forebrain following an axotomy of the ascending monoaminergic fiber system was antagonized by LSD at a dose of 0.5mg/kg i.p. Haloperiodol (2mg/kg i.p.)counteracted the effect of LSD. The increase in dopa formation in corpus striatum and dopamine rich part of the limbic system following treatment with reserpine was antagonized by lisuride as well as LSD. Lisuride was at least 10 times as potent as LSD. In reserpinized animals LSD counteracted the inhibitory effect on dopa accumulation of the direct dopamine receptor stimulant pomorphine while lisuride did not. 31 references. (Author abstract modified)

002169 Keller, H. H.; Burkard, W. P.; Pieri, L.; Bonetti, E. P.; Da Prada, M. Pharmacological Research Department, F. Hoffmann-La Roche & Co. Ltd., Basel, Switzerland **Lisuride- and D-LSD-induced changes of monoamine turnover in the rat brain.** Advances in Biochemical Psychopharmacology. 19:393-396, 1978.

The biochemical effect of lisuride were compared with those of d-lysergic acid diethylamide (LSD) in male albino rats. Lisuride (1mg/kg) induced a decrease in homovanillic acid and 5-hy-

droxytryptamine (5-HT), suggesting a reduction in DA and 5-HT turnover. At low doses, LSD produced similar effects, but a 1mg/kg dose of LSD enhanced DA turnover. Both drugs induced elevated 3-methoxy-4-hydroxyphenylethyleneglycol sulfate and reduced norepinephrine levels, indicating enhanced turnover of norepinephrine. The behavioral effects of the two drugs are also discussed, and it is concluded that lisuride stimulates dopaminergic and serotonergic receptors and blocks noradrenergic receptors. 10 references.

002170 Kelly, P. H.; Moore, K. E. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 **Dopamine concentrations in the rat brain following injections into the substantia nigra of baclofen, gamma-aminobutyric acid, gamma-hydroxybutyric acid, apomorphine, and amphetamine.** Neuropharmacology (Oxford). 17(3):169-174, 1978.

A series of behavioral and biochemical studies were undertaken to examine the effects of baclofen, gamma-aminobutyric acid (GABA), gamma-hydroxybutyric acid (GBH), gamma-butyrolactone (GBL), apomorphine, and d-amphetamine on mesolimbic and nigrostriatal dopaminergic neurons in rat brain. Systemic administration of dl-baclofen and GBL increased the concentration of dopamine (DA) but not of norepinephrine (NE) in rat forebrain. These drugs caused an equivalent increase in DA concentration in the striatum and olfactory tubercle, regions containing terminals of nigrostriatal and mesolimbic dopaminergic neurons respectively. When injected directly into the substantia nigra, GABA, GBH, and baclofen increased DA concentration in the forebrain and apomorphine and d-amphetamine were without effect. When injected into the medial portion of the ventral tegmentum, baclofen increased DA concentration in the olfactory tubercle and nucleus accumbens. Following intracerebral injection, baclofen was several hundred times more potent than GABA, and most of the activity of baclofen resided in the l-isomer. Intracerebral administration of picrotoxin antagonized the ability of GABA but not of baclofen to increase striatal DA concentration. After unilateral injection of GABA, GBH, and baclofen, rats circled away from the side of injection. 36 references. (Author abstract modified)

002171 Khapazhev, T. Sh. Kafedra fiziologii cheloveka i zhivotnykh Kabardino-Balkarskogo gosudarstvennogo universiteta, Nalchik, USSR /**Effect of bromine on the functional interrelationships between the sensorimotor cortex neurons of the rabbit brain.**/ Deystviye broma na funktsional'nyye vzaimootnosheniya neyronov sensomotornoy kory mozga krolika. Zhurnal Vysshey Nervnoy Deyatel'nosti imeni I. P. Pavlova (Moskva). 28(5):1090-1093, 1978.

An experiment was conducted in which bromine was introduced directly onto the surface of the sensory motor cortex of rabbits' brains. This was found to cause a lessening of the number of background active neurons, with a simultaneous lowering of the frequency of their pulsation. The bromine also caused a rise in the level of interaction between neighboring neurons. These results testifies to the direct influence of bromine on the nerve cells of the cortex. The possibility is not excluded that bromine influences the brain by means of iodine exchange in the thyroid gland. 7 references.

002172 Khawaja, Jahangir A.; Wallgren, Henrik; Usmi, Hannu; Hilska, Paivi. Dept. of Medical Chemistry, University of Helsinki, Siltavuorenpenger 10 A, SF-00170 Helsinki 17, Finland **Neuronal and liver protein synthesis in the developing offsprings following treatment of pregnant rats with ethanol or 1,3-butanediol.** Research Communications in Chemical Pathology and Pharmacology. 22(3):573-580, 1978.

Neuronal and liver protein synthesis in the developing offspring were investigated following treatment of pregnant rats with ethanol or 1,3-butanediol. Ethanol or 1,3-butanediol ingestion during pregnancy and lactation results in a marked inhibition of neuronal protein systhesis in the 8-day-old rat progeny, however, the same treatment had a stimulatory effect on the amino acid incorporation by neuronal perikarya of 8-day-old pups. Liver protein synthesis in vitro, on the other hand, was enhanced in both 8 day and 18-day-old pups as a consequence of maternal ethanol consumption. This was attributable to increased aminoacylation in the liver pH 5 enzyme fraction. 15 references. (Author abstract modified)

002173 Kiianmaa, Kalervo. Research Laboratories of the State Alcohol Monopoly (Alko), Box 350, SF-00101 Helsinki 10, Finland **Decreased intoxicating effect of ethanol in rats after 6-hydroxydopamine-induced degeneration of ascending dopamine pathways.** Pharmacology Biochemistry and Behavior. 9(3):391-393, 1978.

To clarify the role of the central dopamine neurons in ethanol intoxication, selective lesions of ascending dopamine pathways were made by bilaterally injecting neurotoxin 6-OHDA (8mcg/4mcl) close to the nigro striatal dopamine pathway of 18 male Long Evans rats. Similar injections were given to 10 control rats. Two months after the operation, intoxication was measured in a tilting plane test after an injection of ethanol (2g/kg, i.p.). Ethanol impaired the performance of the 6-OHDA treated rats significantly less than that of controls. This finding suggests a role for the central dopamine neurons in the intoxicating effect of ethanol. 24 references. (Author abstract modified)

002174 Klaver, M. M.; Flentge, F.; Nienhuis-Kuiper, H. E.; van Praag, H. M. Department of Biological Psychiatry, Psychiatric University Clinic, Oostersingel 59, 9713 EZ Groningen, The Netherlands **The origin of CSF choline and its relation to acetylcholine metabolism in brain.** Life Sciences (Oxford). 24(3):231-236, 1979.

The experimental elevation of serum choline levels in rabbits, induced by intravenous injection of choline or oxotremorine, resulted in a rise in cisternal cerebrospinal fluid (CSF) choline levels. The oxotremorine-induced rise in CSF choline levels could not be attributed to its action on the CNS; this indicates that changes in CSF choline levels may be the result of changes in peripheral choline stores and are not necessarily a reflection of changes in cholinergic activity in the CNS. Isotopic labeling experiments show that the contribution of serum choline to CSF choline was 42%. 18 references. (Author abstract modified)

002175 Klemm, Nikolai; Kuhar, Michael J. Department of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Postmortem changes in high affinity choline uptake.** Journal of Neurochemistry (Oxford). 32(5):1487-1494, 1979.

When the heads of male Sprague-Dawley rats killed by decapitation were kept refrigerated at 2-4 degrees C, high affinity choline uptake was maintained up to 3 days postmortem. At 5 days postmortem, a significant reduction in uptake was observed. In tissues kept at 2-4 degrees for 1 day, the ionic dependence, drug sensitivity, and kinetic parameters of uptake were identical to that of control tissues. At 3 days postmortem, intact synaptosomal profiles with features characteristic of degenerating neuronal tissues were observed in electronmicroscopic studies. In tissues maintained at room temperature, uptake activity disappeared within 1 day. When pentylenetetrazol or pentobarbital were given to rats to activate or depress the choline uptake, activity related changes in choline uptake underwent a reversal in postmortem tissues. Changes in uptake were signifi-

cantly reduced within 10 minutes postmortem and were totally absent by 30 minutes postmortem. In vitro studies with whole hippocampi indicated that the postmortem reversal in activity related changes in uptake is temperature dependent. 21 references. (Author abstract modified)

002176 Klemm, W. R.; Mallari, C. G. Dept. of Biology, Texas A&M University, College Station, TX 77843 **Morphine and naloxone effects on spontaneous unit activity in the caudate, central grey, and amygdala.** Progress in Neuro-Psychopharmacology (Oxford). 2(5/6):535-542, 1978.

Morphine and naloxone effects on spontaneous unit activity in the caudate, central grey, and amygdala regions of the brain were evaluated by monitoring morphine-induced changes in unit pulse activity simultaneously from the three regions at two different times of day in 27 acutely prepared rats. Morphine's principal effect was to depress unit activity in each brain area. Naloxone generally reversed morphine-induced depression, but had no clear effects when given after morphine or after saline had any clear effect on the variance of unit. Neither morphine nor naloxone given after morphine or after saline activity. The relative lack of depression in the anterior amygdala suggests that morphine does not affect all brain areas alike, even when the areas being studied are all thought to be primarily involved in mediating morphine action. The hypothesis that morphine excites neurons there which are inhibitory and thus block transmission of nociceptive input is not supported by the predominance of depression in the central grey region. 26 references. (Author abstract modified)

002177 Kostrzewa, Richard M.; Kastin, Abba J.; Sobrian, Sonya K. Department of Pharmacology, East Tennessee State University College of Medicine, Johnson City, TN 37601 **Potentiation of apomorphine action in rats by L-prolyl-L-leucyl-glycine amide.** Pharmacology Biochemistry and Behavior. 9(3):375-378, 1978.

Potentiation of the action of apomorphine by l-prolyl-l-leucyl-glycine amide (PLG), an antiparkinsonian tripeptide, was demonstrated in the rotational behavior of mature rats which received unilateral 6-OHDA (16mcg) lesions of the striatum as neonates. No change in tyrosine hydroxylase or dopa decarboxylase activities in striatal homogenates were found after addition of PLG. Results suggest that PLG modifies the dopamine receptor, making it more responsive to stimulation by the agonistic agent apomorphine and perhaps by the natural neurotransmitter dopamine. 30 references. (Author abstract modified)

002178 Kozhedub, R. G.; Kozhechkin, S. N.; Voronin, L. L. Otdel problem pamyati Institta biologicheskoy fiziki Akademii nauk SSSR, Pushchino-on-Oka, USSR /**The effect of acetylcholine iontophoresis on cellular and focal septohippocampal reactions.**/ Vliyaniye ionoforeza atsetilkholina na kletochnyye i fokal'nyye septo-gippokampal'nyye reaktsii. Zhurnal Vysshey Nervnoy Deyatel'nosti imeni I. P. Pavlova (Moskva). 28(2):411-414, 1978.

A series of 48 experiments was carried out on 21 rabbits to study the sensitivity to acetylcholine of the spontaneous and evoked reactions of the neurons of the hippocampus. The activity of 54 hippocampal neurons was registered and the influence of ACh iontophoresis on background activity was studied for 36 cells. In 60% of the neurons consistent changes were noted in the frequency of discharge, usually an increase. After septal stimulation late discharges with latent periods of 90-340 msec were registered for 34 neurons. An unexpected effect of the ACh was the heightening of amplitude and area of the fast negative component of the focal potentials. This was explained as the result of an increase in the number of neurons giving early discharges and by the simultaneity and intensity of the discharges. Results of the tests demonstrated a distinct sensitivity of the hippocampal neurons to ACh. 9 references.

002179 Krnjevic, K.; Lamour, Y.; MacDonald, J. F.; Nistri, A. Anaesthesia Research, 3655 Drummond Street, Montreal, Quebec, Canada H3G 1Y6 **Intracellular actions of monoamine transmitters.** Canadian Journal of Physiology and Pharmacology (Ottawa). 56(5):896-900, 1978.

Intracellular injections of noradrenaline (NA) or dopamine (DA) in spinal motoneurons of cats were found to have a clear depolarizing action associated with particularly marked depression of spike potentials and their afterhyperpolarization, but with little slowing down of the falling phase of the action potential. These effects are associated with an increase in input resistance, and they are reversible and reproducible in the same neuron. Intracellular injections of 5-hydroxytryptamine have some depolarizing action and increased input resistance, but they produced no comparable depression of the action potential and tended to enhance the afterpotentials and increase excitability. It is concluded that changes in intracellular levels of monoamines, whether physiological or drug induced, may be of significance for central neuronal function. 18 references. (Author abstract)

002180 Kuhn, Donald Michael. University of South Carolina **Discriminative stimulus properties of LSD: behavioral assay of the mechanism of action of LSD. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 7801157, HC$15. MF$7.50. 98 p. 1977.

The CNS correlates of LSD actions were investigated in a series of experiments by means of a sensitive and specific behavioral assay procedure. Rats, trained to discriminate d-LSD from saline in two lever operant chambers, were injected with .08mg/kg LSD after which reinforcement could only be obtained by responding on one lever; reinforcement on the other lever followed saline injections. Once LSD-saline injections exerted reliable stimulus control over lever choice, rats were tested with various agents which alter the functional activity of the transmitter containing neuronal systems. Treatments with l-tryptophan, cholorimipramine, and Lilly 110140 neither blocked, nor by themselves, mimicked LSD. However, quipazine produced almost complete transfer to LSD. Methiothepin, 2-bromo-d-lysergic acid diethylamide, methysergide, cyproheptadine, and cinanserin blocked the LSD cue in a dose related manner. Haloperidol, fluphenazine, trifuluoperazine, alpha-flupenthixol, and ()-butaclamol were completely without effect on the discriminability of LSD as were alpha-adrenergic antagonists and beta-adrenergic antagonists. Apomorphine produced a partial transfer to LSD. Thus inhibition of raphe (serotonin) unit activity is neither necessary nor sufficient to account for the behavioral effects of LSD, nor is a role for dopamine in mediating the behavioral effects of LSD indicated. The concept of a specific LSD or indole hallucinogen receptor distinct from serotonin dopamine receptors is proposed to account for the results. (Journal abstract modified)

002181 L. Cubeddu, X.; Hoffman, I. S.; Paris, V. B. Universidad Central de Venezuela, Facultad de Farmacia, Farmacologia, Apartado 40109 Nueva Granada, Caracas, Venezuela **Effects of papaverine on the release and metabolism of dopamine in rat striatum.** Journal of Pharmacology and Experimental Therapeutics 209(1):73-78, 1979.

Papaverine (30 and 100mcM) enhanced the basal efflux of radioactive products from rat neostriatal tissue slices prelabeled with tritiated dopamine (3H-DA). This effect was due to a marked, selective increase in the efflux of labeled, 3,4-

dihydroxyphenylacetic acid (3H-DOPAC), which suggests an action of the drug on storage vesicles (granular effect). Papaverine also produced a tenfold increase in the potassium (K) evoked overflow of total 3H and 3H-DA, without affecting the metabolism or the released transmitter; this suggests the drug facilitates neurally mediated transmitter release. A reduction in the tissue content of 3H-DA and a greater proportion of 3H-DOPAC and 3H-O-methylated metabolites were observed after exposure to papaverine. Dibutyryl cyclic adenosine 3',5'-monophosphate and 1-methyl-3-isobutylxanthine did not affect basal of or K stimulated outflow of total 3H, indicating the papaverine's effects on DA release and metabolism are not related to cyclic adenosine monophosphate accumulation. 23 references. (Author abstract modified)

002182 Laduron, P. M., Leysen, J. E. Department of Biochemical Pharmacology, Janssen Pharmaceutica, B-2340 Beerse, Belgium **Is the low incidence of extrapyramidal side-effects of antipsychotics associated with antimuscarinic properties?** Journal of Pharmacy and Pharmacology (London). 30(2):120-122, 1978.

The affinities of various antipsychotic drugs for muscarinic binding sites in rat striatum using radiolabeled dexetimide as ligand and for neuroleptic binding sites using radiolabeled haloperidol as ligand were investigated in vitro in order to determine whether antimuscarinic properties are associated with a low incidence of extrapyramidal side-effects. Clozapine, thioridazine, and perlapine showed a relatively high affinity for the cholinergic receptor as compared with their affinity for 3H-haloperidol binding sites. Pimozide had a low affinity for the cholinergic receptors but a very high affinity for the 3H-haloperidol binding sites. Chlorpromazine, promazine, haloperidol, spiperone, and other drugs with a high incidence of extrapyramidal side-effects showed a dexetimide to haloperidol binding ratio which would make it unlikely that they have pharmacological or clinical antimuscarinic properties. The displacement of 3H-dextimide in various brain areas by clozapine, pimozide, and thioridazine, was also examined in vivo. Clozapine and thioridazine, but not pimozide, displaced the ligand. It is concluded that pimozide, which has a low incidence of extrapyramidal side-effects, does not possess antimuscarinic properties. Possible reasons for the low incidence of extrapyramidal side-effects with pimozide are discussed. 16 references.

002183 Lakshmanan, J. Molecular Biophysics Unit, Indian Institute of Science, Bangalore-560 012, India **Post-synaptic PI-effect of nerve growth factor in rat superior cervical ganglia.** Journal of Neurochemistry (Oxford). 32(5):1599-1601, 1979.

Nerve growth factor (NGF) increased the incorporation of labelled myoinositol into phosphatidylinositol (PI) to 155% of control in Sprague-Dawley rat superior cervical ganglia (SCG). This increase could not be blocked by the muscarinic antagonists atropine and quinuclidinylbenzilate, the nicotinic antagonists d-tubocurarine and chlorisandamine, or the ganglionic blocking agent hexomothonium, indicating that muscarinic and nicotinic cholinergic receptors in the rat SCG are not involved in the mediating the PI effect of NGF. Although the NGF-induced increase in PI turnover was independent of actylcholine release, further experiments with decentralized and sham oparated rats indicated that postsynaptic structures are the primary locus at which NGF elicits the PI effect in rat SCG. 16 references.

002184 Landgren, S.; Backstrom, T.; Kalistratov, G. Department of Physiology, University of Umea, S-901 87 Umea, Sweden **The effect of progesterone on the spontaneous interictal spike evoked by the application of penicillin to the cat's cerebral cortex.** Journal of the Neurological Sciences. 36(1):119-133, 1978.

The effect of intravenous infusion of progesterone and pentobarbital on the frequency and amplitude of the spontaneous interictal spiked from a penicillin focus in the cerebral cortex was investigated in 14 ovariectomized cats anesthetized with chloralose. The plasma concentration of progesterone was determined. It was found that the generation of penicillin spikes was depressed by progesterone in plasma concentrations as low as 40ng/ml. Equimolar doses of pentobarbital were less effective. 44 references. (Author abstract)

002185 Lazarus, J. H.; Muston, H. L. Dept. of Medicine, University Hospital of Wales, Heath Park, Cardiff, Wales **The effect of lithium on the iodide concentrating mechanism in mouse salivary gland.** Acta Pharmacologica et Toxicologica (Kobenhavn). 43(1):55-58, 1978.

The iodide concentrating mechanism, measured as the gland to plasma iodide concentration ratio, was measured in male mouse submandibular glands after the animals had been fed with varying amounts of lithium chloride for intervals ranging from 0 to 8 weeks. After acute exposure (by injection) to lithium, the concentration ratio fell compared to control values and was further depressed at high serum lithium values. Chronic exposure to lithium was characterized by an increase in the concentration ratios at therapeutic serum lithium concentrations. It is suggested that lithium has a direct effect on the iodide concentrating mechanism that may be independent of any action of thyroid stimulating hormone during this process. 20 references. (Author abstract modified)

002186 Lee, C. M.; Wong, P. C. L. MRC Neurochemical Pharmacology Unit, Department of Pharmacology, Medical School, Hills Road, Cambridge CB2 2QD, England **Effects of morphine on the rat striatal dopamine metabolism.** Biochemical Pharmacology (Oxford). 28(2):163-170, 1979.

Intracarotidly administered morphine (5mg/kg) totally suppressed the spontaneous unitary discharges of neurons in the male Sprague-Dawley rat corpus striatum and increased the levels of dopamine, homovanillic acid, and cyclic adenosine monophosphate (AMP) by 80, 65, and 46%, respectively. Morhpine did not alter the activity of striatal tyrosine aminotransferase or tyrosine hydroxylase. Morphine did not interfere with the inhibitory effects of dopamine on striatal tyrosine hydroxylase in vitro, but it significantly potentiated the stimulatory effects of cyclic AMP on this enzyme. Morphine had no effect on the spontaneous or potassium stimulated release of dopamine from striatal homogenates and synaptosomes, but did inhibit the uptake of dopamine by these preparations; naloxone did not reverse the morphine-induced inhibition of dopamine uptake. Results indicate that acutely administered morphine stimulates the dopaminergic pathway by prolonging the effect of dopamine on postsynaptic neurons and by decreasing presynaptic cytosol dopamine thus leading to increased synthesis of dopamine. 54 references. (Author abstract modified)

002187 Lettieri, John; Fung, Ho-Leung. Department of Pharmaceutics, School of Pharmacy, SUNY at Buffalo, Amherst NY 14260 **Improved pharmacological activity via pro-drug modification: comparative pharmacokinetics of sodium gamma-hydroxybutyrate and gamma-butyrolactone.** Research Communications in Chemical Pathology and Pharmacology. 22(1):107-118, 1978.

Although gamma-butyrolactone (GBL) rapidly converts to gamma-hydroxybutyrate (GHB) in vivo, the lactone gave significantly more prolonged hypnotic effect than GHB when equimolar doses were compared after oral of parenteral administration to male Sprague-Dawley rats. Plasma drug concentrations were higher after GBL administration by both routes, consistent with the observed differences in the pharmacological ac-

tivity of the two compounds. Oral GBL was absorbed much faster than oral GHB, with th dual effects of decreasing potential first pass metabolism and elevating plasma drug concentrations to the region where capacity limited elimination is operative. Parenteral GBL produced a slower initial drug plasma clearance than parenteral GHB. In spite of the rapid metabolism of GBL to GHB, the apparent tissue distribution of these two compounds may be different. 15 references. (Author abstract)

002188 Leysen, J. E.; Gommeren, W.; Laduron, P. M. Dept. of Biochemical Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Endogenous ligands for CNS drug receptors?** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 236(2):310-314, 1978.

A number of beta-lipotropin (beta-LPH) fragments, or endorphins were tested in different models of central drug receptors, and in a separate study, a macromolecule able to mask various drug receptors was detected. Among the beta-LPH fragments which were tested on various receptor models, alpha-endorphin was found to bind with moderate affinity to the opiate receptor; none of the other peptides showed high binding affinity for any of the receptors, neither at 37 degrees C nor at 0 degrees C nor in the presence of bacitracine. High molecular weight factors which can mask 3H-ligand binding to at least four different CNS receptors were found to be present in various rat brain areas. It is hypothesized that these factors are macromolecules which do not specifically bind to the receptor sites, but which may form a covering layer over membranes in a way that prevents access to the specific sites. 14 references.

002189 Liang, Chi-Ming. University of Arkansas for Medical Sciences **Tricyclic antidepressants and dual ganglionic impulse transmission. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 7800330, HC$15. MF$7.50. 169 p. 1978.

To investigate the relationship between tricyclic antidepressants and dual ganglionic impulse transmission, heartrate was increased by either electric stimulation of sympathetic cardiac nerve or close intraarterial injection of ganglionic stimulants in the dog spine. Neither hexamethonium, a nicotinic blocking drug, nor atropine, a muscarinic blocking drug, could completely block the cardiac response to preganglionic nerve stimulation; however, the response was abolished by the combination of C6 and atropine, indicating that there is a dual ganglionic impulse transmission, via nicotinic receptors blocked by C6 and via muscarinic ones blocked by atropine. The response of preganglionic nerve stimulation was depressed by dopamine in a dose dependent manner. Tricyclic antidepressants, desipramine (DMI) and nortriptyline depressed both the C6 resistant response to preganglionic stimulation and the response to McNeil A-343, a muscarinic agonist. The ganglionic action of DMI was prevented by phentolamine. It is suggested that DMI attenuates ganglionic muscarinic transmission indirectly by potentiating the inhibitory action of the intraganglionic catecholamine system. (Journal abstract modified)

002190 Lin, M. T.; Chow, C. F.; Chern, Y. F. Dept. of Biophysics and Physiology, National Defense Medical Center, Taipei, Taiwan **The effects of a decarboxylase inhibitor, benserazide, on both thermoregulation and chlorpromazine-induced hypothermia in rats.** Journal of Pharmacy and Pharmacology (London). 30(12):759-761, 1978.

Pretreatment with benserazide, a peripheral decarboxylase inhibitor, greatly enhanced with hypothermia induced by chlorpromazine in male Sprague-Dawley rats at room temperature. Benserazide alone produced alterations in body temperature that were dependent on ambient temperature. In the cold, the drug-induced hypothermia brought about by a decrease in heat production. At room temperature, a dose dependent hypothermia was preceded by a slight hyperthermia; the hyperthermia was due to an increase in skin temperature and a decrease in metabolic heat production, while the hyperthermia was due to a decrease in skin temperature and an increase in metabolic heat production. In the heat, hyperthermic responses to benserazide were associated with decreases in skin temperature. Benserazide had no significant effect on brain serotonin content. 14 references. (Author abstract modified)

002191 Lindquist, Thomas D.; Ingoglia, Nicholas A. Department of Physiology, New Jersey Medical School, Newark, NJ 07103 **Evidence that 4S RNA is axonally transported in normal and regenerating rat sciatic nerves.** Brain Research (Amsterdam). 166(1):95-112, 1979.

To determine if ribonucleic acid (RNA) is axonally transported in normal or regenerating mammalian peripheral nerves, Sprague-Dawley male rats were given bilateral intravenous or intraspinal injections of tritiated uridine 10 days after unilateral sciatic nerve crush. The intraspinal injections of (3H)uridine were used to label Schwann cell RNA as well as axonal RNA, whereas intravenous injections were expected to label only Schwann cell RNA. An enrichment of 4S RNA was observed in both normal and regenerating sciatic nerves following intraspinal but not intravenous injection of the labeled precursor. These results suggest that 4S RNA migrates axonally in both normal and regenerating sciatic nerves of rats. 38 references. (Author abstract modified)

002192 Liu, Shean-Jang; Evans, David B.; Wang, Richard I. H. Pharmacology Research Laboratories, Veterans Administration Center Wood, Milwaukee, WI **Analysis and differentiation of mechanism of tolerance to methadone in methadone-fed rats.** Biochemical Pharmacology (Oxford). 28(2):287-293, 1979.

Male Sprague-Dawley rats fed methadone in drinking water (0.5mg/ml) for 1 or 2 weeks developed tolerance to the analgesic effect of methadone, accompanied by increased methadone N-demethylase activity in vitro and increased methadone metabolism in vivo. Two day oral methadone administration and four day phenobarbital pretreatment also increased methadone metabolism in vitro and in vivo and decreased the analgesic effect of methadone but not of morphine. Methadone fed rats also developed cross-tolerance to morphine-induced analgesia. Two week feeding caused tolerance to the analgesic effects of methadone and morphine to a greater degree than one week feeding, but no significant differences were found between increases in methadone metabolism produced by 1 and 2 week feedings. Results suggest that tolerance to methadone analgesia induced by chronic methadone feeding is due to increased metabolic inactivation of methadone, as well as cellular adaptation to the drug in the brain. 34 references. (Author abstract modified)

002193 Lorden, Joan F.; Dawson, Ralph, Jr.; Callahan, Michael. Dept. of Psychology, University of Alabama, Birmingham, AL 35294 **Effects of goldthioglucose lesions on central catecholamine levels in the mouse.** Pharmacology Biochemistry and Behavior. 10(1):165-169, 1979.

Quantitative biochemical assay procedures were used to assess damage to catecholamine systems in goldthioglucose (GTG) induced obesity in male and female C57B1/6J mice. Significant increases in bodyweight were inversely correlated with pituitary dopamine (DA) levels. Significant reductions in hypothalamic norepinephrine (NE) and DA were also noted, but these reductions did not appear to be related to bodyweight gain. The GTG injections did not produce any significant alterations in telencephalic NE or DA. The damage to catecholamine neurons

is discussed in relation to the endocrine abnormalities of the GTG mouse and to current hypotheses of control of food intake. 38 references. (Author abstract modified)

002194 Loscher, W. Dept. of Pharmacology and Toxicology, Free University of Berlin, School of Veterinary Medicine, Koserstrasse 20, D-1000 Berlin 33, Germany **GABA in plasma and cerebrospinal fluid of different species. Effects of gamma-acetylenic GABA, gamma-vinyl GABA and sodium valproate.** Journal of Neurochemistry (Oxford). 32(5):1587-1591, 1979.

Gamma-aminobutyric acid (GABA) concentrations in cerebrospinal fluid (CSF) and plasma of dogs, rats, and cats were determined. The concentration of GABA in CSF of dogs and cats compared well with reported values for humans, but the concentration in rats was somewhat lower. Plasma GABA content was similar in rat, cat, and dog, but lower in humans. GABA was present in lower concentrations in CSF than in plasma, but no correlation between plasma and CSF GABA concentrations was found in any species. In further studies in dogs, gamma-acetylenic GABA increased both plasma and CSF GABA in a dose dependent manner. Administration of gamma-vinyl GABA or sodium valproate elevated CSF GABA levels in CSF but not in plasma. Results suggest that GABA CSF determinations may be a useful tool to monitor changes of brain GABA content, whereas measurement of GABA in plasma may be helpful only in the instances in which brain and blood GABA are known to increase to a similar extent. 38 references.

002195 Loscher, W.; Esenwein, H. Freie Universitat, Fachbereich Veterinarmedizin, Lab. fur Pharmakologie und Toxikologie, Koserstrasse 20, D-1000 Berlin 33, Germany **Pharmacokinetics of sodium valproate in dog and mouse.** Arzneimittel Forschuung (Aulendorf). 28(5):782-787, 1978.

The pharmacokinetics of sodium di-n-propylacetate (sodium valproate, or Ergenyl) after i.v. and oral administration in dogs and mice were studied. After i.v.,20 and 40mg/kg doses in dogs caused a biphasic exponential decay of valproate serum concentrations, suggesting a two compartment open model. With mice, a monophasic exponential decay of valproate serum concentrations occurred after 200 and 420mg/kg i.v. administration, corresponding to a one compartment open model. Valproate was rapidly eliminated in both species, with a half-life of 90-120 min in dogs and 50 min in mice. Valproate was readily absorbed in both species after oral administration. Transfer from blood to brains in mice was likewise rapid, and the observed concentrations in the brain were 1/4 to 1/5 of that in serum. The bonding of valproate to serum proteins in dog serum was calculated to 88%. The pKa of valproate was 4.56 and valproate was, therefore, nearly lipid insoluble at pH 7.4. 13 references. (Author abstract modified)

002196 MacDonald, Robert L.; Barker, Jeffery L. University of Michigan, Department of Neurology, Neurosciences Laboratory Building, 1103 East Huron, Ann Arbor, MI 48109 **Enhancement of GABA-mediated postsynaptic inhibition in cultured mammalian spinal cord neurons: a common mode of anticonvulsant action.** Brain Research (Amsterdam). 167(2):323-336, 1979.

Murine spinal cord neurons grown in dissociated cell culture were used to study the effects of barbiturate (phenobarbital and mephobarbital) and benzodiazepine (diazepam and chlordiazepoxide) anticonvulsants on amino acid responses. Both types of anticonvulsant augmented postsynaptic inhibition mediated by gamma-aminobutyric acid (GABA), but not by glycine or beta-alanine. Barbiturates, but not benzodiazepines, antagonized glutamate mediated postsynaptic excitation. It is suggested that the augmentation of GABA mediated inhibition by these drugs contributes to their anticonvulsant action and that the antagonism of glutamate mediated excitation contributes to the anticonvulsant and sedative actions of the barbiturates. 71 references. (Author abstract modified)

002197 MacKenzie, R. G.; Trulson, M. E. Program in Neuroscience, Department of Psychology, Princeton University, Princeton, NJ 08540 **Reduced sensitivity to L-tryptophan and parachloroamphetamine in streptozotocin-diabetic rats.** Journal of Pharmacy and Pharmacology (London). 30(2):131-132, 1978.

The sensitivities of normal rats and of rats made diabetic by administration of streptozotocin to two treatments capable of inducing a behavioral syndrome that reflects the activity in central serotonin (5-HT, 5-hydroxytryptamine) mediated synapses was investigated. The study was carried out to determine whether the restriction of tryptophan accumulation in the brain which occurs in diabetics has a functional significance regarding the activation of 5-HT receptors. Following inhibition of monoamine oxidase with pargyline, the dose response curve for the induction of the behavioral syndrome in diabetic rats by L-tryptophan exhibited a large shift to the right as compared with data for normal rats. It is suggested that this reduced behavioral responsiveness in diabetic rats is due to restricted central accumulation of tryptophan. However, the dose response curve for the induction of the behavioral syndrome in diabetic rats by parachloroamphetamine (PCA) was also shifted to the right as compared with controls. Since diabetes does not significantly alter the brain uptake of amphetamine, it is proposed that the mechanism for subsensitivity to PCA in diabetic rats remains to be determined. 9 references.

002198 Mackenzie, Robert George. Princeton University **The effects of diabetes and insulin on brain tryptophan and serotonin metabolism. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 7818375, HC$15. MF$7.50. 101 p. 1978.

A series of experiments were undertaken to examine the effects of insulin and streptozotocin-induced diabetes on brain tryptophan (TRY) concentrations and serotonin (5-hydroxytryptamine, 5-HT) metabolism in rats. In experiment 1, a TRY deficit in diabetic rats which can be reversed by systemic administration of insulin was demonstrated. Insulin also increased TRY concentrations in normal rats. Experiment 2 demonstrated that insulin controls TRY levels by affecting the ratio of TRY plasma concentration to the sum of plasma concentrations of the other large neutral amino acids which compete with TRY for central uptake. Insulin injection increased and diabetes decreased this ratio. Diabetes severely restricted the increase in brain TRY, 5-HT, and 5-hydroxyindoleacetic acid following systemic TRY load, as shown in Experiment 3. Experiment 4 showed that the restricted central accumulation of TRY in diabetes leads to a reduced production of functional 5-HT. Experiment 5 indicated that diabetes has no effect on tryptophan hydroxylase activity. In conclusion, the experiments underline the importance of the action of insulin on the plasma balance of amino acids in the control of brain tryptophan and 5-HT metabolism and suggest how alterations in plasma insulin levels could effect central nervous system function. (Journal abstract modified)

002199 Mackerer, Carl R.; Kochman, Ronald L. Department of Biological Research, Searle Laboratories, Chicago, IL 60680 **Effects of cations and anions on the binding of 3H-diazepam to rat brain.** Proceedings of the Society for Experimental Biology and Medicine. 158(3):393-397, 1978.

The effects of anions and cations on the specific binding of tritiated diazepam to synaptosomal fractions of male CR-CD rat whole brain were determined. The monovalent cations (as their

chloride salts) lithium, sodium, potassium, and ammonium produced very slight enhancements of binding, whereas cesium had no effect. The monovalent anions (as their sodium salts) fluorine and iodine were inhibitory, but bromine produced a very slight enhancement. Divalent cations (as their chloride salts) produced marked enhancements of binding; nickel caused the greatest increase (86% at 5mM). This increased binding was the result of enhanced affinity for the binding site; the total number of binding sites was not altered. Nickel did not affect the specific binding to brain homogenates of tritiated strychnine or quinuclidinyl benzilate, but inhibited the binding of tritiated naloxone. 16 references. (Author abstract modified)

002200 MacMillan, V. Dept. of Medicine (Neurology), Rm. 7214, Medical Sciences Bldg., University of Toronto, Toronto, Ontario, Canada M5S 1A8 **The effects of acute hypercapnia on cerebral indole amine metabolism.** Canadian Journal of Physiology and Pharmacology (Ottawa). 56(2):223-226, 1978.

The effects of 1 hour's exposure to hypercapnia (PaC02, 90mmHg to 110mmHg) on cerebral indoleamine metabolism were studied in rats by measurement of cerebral hemisphere contents of tryptophan, 5-hydroxytryptophan (5-HTP), 5-hydroxytryptamine (5-HT), and 5-hydroxindoleacetic acid (5-HIAA). The 5-HIAA content was increased after 1 hour's exposure to hypercapnia, whereas tryptophan, 5-HTP, and 5-HT remained unchanged from control values. The accumulation of 5-HTP after decarboxylase inhibition with 3-hydroxybenzyl hydrazine was increased in hypercapnic rats and indicated heightened tryptophan hydroxylase activity. During the 1 hour's exposure to hypercapnia, there was increased accumulation of 5-HT after monoamine oxidase inhibition with pargyline, and increased accumulation of 5-HIAA after probenecid. Results indicate an increased synthesis and degradation of indoleamines in acute hypercapnia. 22 references. (Author abstract)

002201 Malfroy, B.; Swerts, J. P.; Guyon, A.; Roques, B. P.; Schwartz, J. C. Unite 109 de Neurobiologie, Centre Paul Broca de l'INSERM, 2ter rue d'Alesia F-75014 Paris, France **High-affinity enkephalin-degrading peptidase in brain is increased after morphine.** Nature (London). 276(5687):523-526, 1978.

Evidence for the presence of a high-affinity peptidase in a particulate fraction of mouse striatum splitting the Leu-enkephalin molecule with release of a tripeptide fragment (Tyr-Gly-Gly) and exhibiting definite substrate specificity is presented. The marked and selective increase in the activity of this peptidase in the striatum of mice chronically treated with morphine suggests that it might be associated with enkephalingeric transmission. The details of this activity are described, and implications for development of a new class of therapeutic agents (enkephalinase inhibitors) exhibiting opiate-like properties are suggested. 13 references.

002202 Malick, Jeffrey B. Biomedical Research Department, ICI Americas Inc., Wilmington, DE 19897 **Antidepressants: potential utility in the treatment of chronic pain and the terminally ill.** Archives of the Foundation of Thanatology. 7(1):39, 1978.

In a summary of a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, the effects of antidepressants from various chemical classes on several laboratory analgesic models, writhing procedures, tail flick, and Randall Selitto inflamed paw test, were examined using mice. Previous report have impled that the ability of the tricyclics to inhibit amine uptake was their mechanism of action as analgesics. However, in the present study, iprindole, a nontricyclic antidepressant that is not an uptake inhibitor, also exhibited analgesic activity. Chronic pain in man may lead to profound mental depression, and emotions may influence pain perception. It is concluded that in patients suffering chronic pain, antidepressants may be very useful in treating both the pathologically-induced pain and the associated emotional complications.

002203 Maoi, Makoto; Suzuki, Tatsuo, Yagi, Kunio. Institute of Biochemistry, Faculty of Medicine, University of Nagoya, Nagoya 466, Japan **Effects of chlorpromazine and other phenothiazine derivatives on the permeability of liposomes.** Biochemical Pharmacology (Oxford). 28(2):295-299, 1979.

Chlorpromazine and other phenothiazine derivatives increased the permeability of liposomes to D-glucose and D-amino acids. The presence of a halogen atom at the C-2 position of the phenothiazine nucleus increased this effect. The lipid composition of liposomes influenced the effects of the phenothiazine derivatives; the incorporation of cholesterol into the membrane reduced the drug effects. Phenothiazines did not release the macromolecular marker D-glucose oxidase or D-amino oxidase from the liposomes. 11 references. (Author abstract modified)

002204 Marangos, P. J.; Paul, S. M.; Parma, A. M.; Goodwin, F. K.; Syapin, P.; Skolnick, P. NIMH, 9000 Rockville Pike, Bethesda, MD 20014 **Purinergic inhibition of diazepam binding to rat brain (in vitro).** Life Sciences (Oxford). 24(9):851-857, 1979.

A wide spectrum of purines inhibited specific tritiated diazepam binding to Sprague-Dawley rat brain synaptosomes, but pyrimidines were inactive. Preliminary structure activity relationships indicate that the 2'-deoxypurines and 1-methyl compounds are particularly potent inhibitors of diazepam binding, while the 7-methyl purines are inactive. The xanthine stimulants caffeine, theophylline and theobromine competitively inhibited (3H)diazepam binding, as did the CNS convulsant pentylenetetrazol. 16 references. (Author abstract modified)

002205 Mason, Stephen T.; Corcoran, Michael E. Division of Neurological Sciences, Dept. of Psychiatry, University of British Columbia, Vancouver, BC, V6T 1W5, Canada **Seizure susceptibility after depletion of spinal or cerebellar noradrenaline with 6-OHDA.** Brain Research (Amsterdam). 166(2):418-421, 1979.

Seizure susceptibility was examined in male Wistar rats depleted of spinal or cerebellar noradrenaline (NA) by intracerebral injection of 6-hydroxydopamine. Depletion of spinal NA abolished the decapitation reflex, potentiated the convulsions induced by electroconvulsive shock, and had no effect on seizures induced by metrazol. Depletion of cerebellar NA did not alter seizures in any of these models. Results indicate that the descending NA innervation to the spinal cord plays a role in convulsions different from that of the ascending NA innervation to the forebrain. Cerebellar NA innervation is apparently not involved in convulsions in any major fashion. 16 references.

002206 Mason, Stephen T.; Iversen, Susan D. Division of Neurological Sciences, Dept. of Psychiatry, University of British Columbia, Vancouver, British Columbia V6T 1W5, Canada **Reward, attention and the dorsal noradrenergic bundle.** Brain Research (Amsterdam). 150(1):135-148, 1978.

The hypothesis that the resistance to extinction seen after lesion to the dorsal noradrenergic bundle arises from a deficit in internal inhibition or a perseverative type of deficit was tested by examining the ability of 6-hydroxydopamine treated rat pups to inhibit a previously developed preference for saccharine solution as a result of poisoning with lithium chloride. Unimpaired taste aversion was found, arguing against a deficit in the ability to inhibit a prepotent response. An alternative explanation of the

dorsal bundle extinction effect, that of alterations in attention, was tested by acquisition and reversal of a successive light/dark discrimination. Both acquisition and reversal were severely impaired, suggesting that the treated animals have difficulty in attending to a specific stimulus in the environment when this is required in order to structure behavior appropriately. This is viewed as being consistent with a role for the dorsal bundle in the control of attentional processes. 50 references. (Author abstract)

002207 Matsui, Yoshiki; Kamioka, Toshiharu. Central Research Laboratories, Sankyo Co., Ltd., Hiromachi 1-chome Shinagawa-ku, Tokyo 140, Japan **Cataleptic and anticataleptic effects of muscimol and gabaculine injected into globus pallidus and substantia nigra, and interactions with haloperidol or benzodiazepines.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 305(3):219-225, 1978.

The functional role of the GABA-ergic systems in substantia nigra and globus pallidus in catalepsy and the interactions of benzodiazepines with pullidal GABA mechanisms were studied. Intranigral injection of muscimol-induced hyperactivity in rats and antagonized haloperidol-induced catalepsy. Three benzodiazepines, nitrazepam, diazepam, and chlordiazepoxide administered orally, potentiated the effect of muscimol injected into the globus pallidus and induced catalepsy. It is suggested that stimulation of GABA receptor or increase of GABA content in the substantia nigra antagonize haloperidol-induced catalepsy by activation of nigral dopaminergic system, and that enhancement of pallidal GABA function induces catalepsy by nondopaminergic mechanisms. Potentiation of haloperidol-induced catalepsy by benzodiazepines may be due to enhancement of GABA-ergic transmission within the globus pallidus. 36 references. (Author abstract modified)

002208 Matsuzaki, M. Nippon Merck-Banyu Research Institute, Okazaki City, Japan **Alteration in pattern of EEG activities and convulsant effect of cocaine following chronic administration in the Rhesus monkey.** Electroencephalography and Clinic Neurophysiology (Amsterdam). 45(1):1-15, 1978.

The effects of chronic administration of high doses of cocaine were studied in monkeys with electrodes implanted in the brain, focusing on alteration of EEG and convulsive behavior. Ss were injected daily at a minimal convulsant dose during polygraphic recording of EEGs, eye movement. respiration, and heartrates. The pattern of daily convulsions changed from multiple episodes of intermittent tonic/clonic convulsions, which occurred during the earlier stage of chronic treatment, to a single episode of sustained tonic/clonic convulsion. Ss became placid and tame or were profoundly depressed in overall behavior most of the time. Simultaneously, Ss continuously showed persistent rhythmic slow waves predominantly in the neocortex and limbic system structures. Results strongly suggest that chronic cocaine administration at high doses causes relatively permanent alteration of EEGs and behavior in the Ss, and that the limbic system structures play an important role in this effect. 40 references. (Author abstract modified)

002209 McGeer, E. G.; McGeer, P. L. Department of Psychiatry, University of British Columbia, Vancouver, British Columbia, Canada V6T 1W5 **Localization of glutaminase in the rat neostriatum.** Journal of Neurochemistry (Oxford). 32(3):1071-1075, 1979.

Lesions of the corticostriatal trace in male Wistar rats depressed striatal glutamate uptake by 47%, but did not significantly depress glutaminase activity in the striatum. However, intrastriatal kainic acid injections markedly decreased striatal glutaminase activity. There appeared to be a linear correlation between the glutaminase and glutamic acid decarboxylase activities in the substantia nigra of rats treated with kainic acid. Results suggest that most of the glutaminase activity in these regions is localized in structures containing gamma-aminobutyric acid and provide no evidence for the occurrence of this enzyme in nerve endings of the glutamergic corticostriatal tract. 21 references. (Author abstract modified)

002210 Messiha, F. S. Dept. of Pathology and Psychopharmacology Laboratory, Dept. of Psychiatry, Texas Tech University School of Medicine, Lubbock, TX 79409 **Cesium and rubidium salts: effects on voluntary intake of ethanol by the rat.** Pharmacology Biochemistry and Behavior. 9(5):647-651, 1978.

The effects of cesium and rubidium salts on voluntary intake of ethanol solution by rats preferring ethanol solution (5%) over water as the drinking fluid was studied as a function of the dose given and the vehicle injected. Administration of small amounts of the salts for three consecutive days, did not alter amounts of ethanol consumed, but repeated administration of larger doses for 3 days produced some moderate reduction in ethanol consumption. Simultaneous injection of cesium and rubidium salts resulted in greater and profound lasting decreases in ethanol drinking. In general, dissolving the chloride salt of the alkali metals in saline resulted in greater effects on ethanol drinking than that determined after identical doses injected with water as the vehicle. 31 references. (Author abstract modified)

002211 Middaugh, Lawrence D.; Boggan, William O.; Wilson-Burrows, Carolyn; Zemp, John W. Dept. of Biochemistry, Medical University of South Carolina, Charleston, SC 29401 **Prenatal maternal phenobarbital alters plasma concentrations of corticosterone in developing offspring.** Life Sciences (Oxford). 24(11):999-1002, 1979.

Offspring of C57BL/6J mice injected daily with phenobarbital during the last third of pregnancy had elevated concentrations of corticosterone on the day of birth and reduced concentrations 21 days after birth. The high concentration at birth is compatible with literature suggesting a compensatory increase in fetal corticosterone due to reductions in maternal corticosterone. The lower concentration of corticosterone at 21 days of age is compatible with reports on the effects of neonatal injections of corticosterone on plasma concentrations of the glucocorticoid in young rats. 26 references. (Author abstract)

002212 Millington, William R.; McCall, Anthony L.; Wurtman, Richard J. Dept. of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, MA 02139 **Deanol acetamidobenzoate inhibits the blood-brain barrier transport of choline.** Annals of Neurology. 4(4):302-306, 1978.

Competition by deanol (dimethylaminoethanol) with choline for uptake from the bloodstream into the brain was investigated. Methods included the simultaneous intracarotid administration (in rats) of carbon 14-labeled choline with deanol (plus tritiated water and indium 113m, to calculate a brain uptake index) and measuring the brain uptake of 14C-labeled choline mixed with sera from rats pretreated with deanol. The inhibition constant for inhibition of choline uptake by deanol was actually lower than the Michaelis constant for choline itself; hence, the affinity of the carrier mechanism for deanol is at least as great as it is for choline. Deanol administration also elevated blood choline levels; thus, the effect of the drug on brain choline (and acetylcholine) levels is the result of the increase it produces in blood choline and the suppression it causes in choline uptake. The findings are discussed in relation to discrepant results from laboratories seeking increases in brain acetylcholine or clinical improvement in patients with tardive dyskinesia after deanol treatment. 29 references. (Author abstract)

002213 Minchin, M. C. W. Department of Physiology, University of Sheffield, Sheffield S10 2TN, England **Uptake of (14C)nipecotic acid into rat dorsal root ganglia.** Journal of Neurochemistry (Oxford). 32(5):1519-1524, 1979.

Radioactive nipecotic acid accumulated in isolated, desheathed male Wistar rat dorsal root ganglia by a saturable process with an apparent Michaelis-Menten constant of 48.8mcM and maximum velocity of 2.2nmol/g/minute. Beta-alanine and L-2, 4-diaminobutyric acid (L-DABA) both inhibited uptake of nipecotic acid, but the concentration of L-DABA required to inhibit uptake by 50% was three times greater than that of beta-alanine. Light microscopic autoradiography indicated that the sites of uptake of (14C)nipecotic acid were principally confined to satellite glial cells. It is concluded that nipecotic acid is transported by the GABA uptake system in glia, but that it has less affinity for this system than GABA does. 10 references. (Author abstract modified)

002214 Mitchell, P. R.; Martin, I. L. MRC Neuropharmacology Unit, Medical School, Birmingham, England **The effects of benzodiazepines on K-stimulated release of GABA.** Neuropharmacology (Oxford). 17(4/5):317-320, 1978.

The effects of the benzodiazepines diazepam and flurazepam on the in vitro potassium (K) stimulated release of tritiated gamma-aminobutyric acid (GABA) were investigated in male Wistar rat cortical tissue. A facilitation of K stimulated (3H)GABA release was seen at low benzodiazepine concentrations (0.000001M), which is of the same order as that previously found to protect against pentylenetetrazol-induced convulsion in vivo. At a much higher concentration (0.0001M), the benzodiazepines inhibited release of (3H)GABA. (Author abstract modified)

002215 Mitchell, P. R.; Martin, I. L. no address **Is GABA release modulated by presynaptic receptors?** 274(5674):904-905, 1978. MRC Neuropharmacology Unit, Medical School, Birmingham, England

In a study of the modulation of GABA release by presynaptic receptors, the effects of GABA agonists, antagonists, and GABA itself on the release of GABA from in vitro rat frontal cortex caused by elevated potassium ion concentrations were investigated. It is reported that release of GABA is reduced by the GABA agonists muscimol and 3-aminopropane sulphonic acid, and by GABA itself, and also that the effect of muscimol is antagonized by the GABA antagonists bicuculline and picrotoxin. Results demonstrate that the release of GABA is subject to a negative feedback control which may be important in vivo, and further, that this mechanism can be modified by drugs. 18 references.

002216 Moleman, Peter; Bruinvels, Jacques; van Valkenburg, Cornelis F. M. Dept. of Psychiatry, Academic Hospital Dijkzigt, Dr Molewaterplein 40, Rotterdam, The Netherlands. **Haloperidol inhibits the disappearance of acidic dopamine metabolites from rat straitum.** Journal of Pharmacy and Pharmacology (London). 30(9):583-585, 1978.

To test whether the increase in the acidic metabolites homovanillic acid (HVA) and 3,4-dihydroxyphenyl acetic acid (DOPAC) by haloperidol results from the inhibition of the transport of these metabolites, the formation of acidic metabolities was inhibited with pargyline and the effect of haloperidol on the metabolite concentrations was studied. Similarly, the effect of the dopamine agonist apomorphine was studied. Results show that haloperidol strongly inhibits the transport or disappearance of the acidic dopamine metabolites HVA and DOPAC from the rat striatum. 16 references.

002217 Moore, R. H.; Domino, E. F. Kirksville College of Osteopathic Medicine, Dept. of Physiology, Kirksville, MO 63501 **Modification of the effects of LSD-25, d-amphetamine and tryptamine on electrically evoked responses in the visual system by methiothepin and octoclothepin.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 236(1):66-73, 1978.

The ability of methiothepin and octoclothepin to block the actions of LSD-25, d-amphetamine, and tryptamine on electrically evoked visual responses in cats was examined. LSD-25, d-amphetamine, and tryptamine given intravenously depressed the response recorded in the visual cortex to electrical stimulation of the optic chiasm of the chloralose anesthetized cat. Relatively large doses of the dibenzothiepin derivatives, methiothepin and octoclothepin, antagonized the depressant effects of both LSD-25 and tryptamine to a greater degree than d-amphetamine. It is concluded that the data are consistent with the hypothesis that some neuroleptic drugs in large dosage like the dibenzothiepins studied do antagonize tryptaminergic hallucinogens. 10 references. (Author abstract modified)

002218 Morinan, Alun. Dept. of Pharmacology, University College, Galway, Northern Ireland **Social isolation in the young rat: neurochemical correlates of chronic amphetamine treatment.** Irish Journal of Medical Science (Dublin). 147(Supplement 1):53-56, 1978.

A paper read at the first Irish Psychopharmacology Conference, held in Belfast in March 1978, is presented. The neurochemical changes induced by chronic treatment with d-amphetamine in rats housed individually or in groups of four were assessed. Alteration in GABA, DA, and NA brain concentrations wre independent of environmental treatment. Changes in 5-HT, DA, and NA were dependent on the housing condition. These findings attest to the diverse influence of amphetamine on brain biogenic amines, but more importantly, that modification of the environment can alter the effect of this drug on these systems. 12 references. (Author abstract modified)

002219 Moroni, F.; Peralta, E.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Turnover rates of GABA in striatal structures: regulation and pharmacological implications. (Unpublished paper).** Bethesda, MD, NIMH, 1978. 17 p.

Information acquired when measuring the turnover rate of GABA in an examination of striatal GABAergic mechanisms is reported. The experiments using the described methodology reveal that there is no direct synaptic connection between dopaminergic terminals and GABA neurons in striatum, and that this direct connection probably exists in the N. accumbens. Furthermore, the increased turnover rate of striatal DA caused by all the antipsychotics given in single doses is not caused by a decreased utilization rate of GABA in substantia nigra. Data indicate that the decreased ability of thioridazine and clozapine to cause extrapyramidal side-effects may be related to an increase in GABA utilization elicited by both drugs in substantia nigra. Interactions between enkephalinergic and GABAergic neurons are also examined. 22 references.

002220 Muraki, Takamura; Tokunaga, Yukiko. Department of Pharmacology, School of Medicine, Keio University, Shinanomachi, Shinjuku-ku, Tokyo 160, Japan **Effects of morphine on the serum prolactin levels of morphine-tolerant and nontolerant male rats and on the in vitro release of pituitary prolactin.** Japanese Journal of Pharmacology (Kyoto). 28(6):803-810, 1978.

Morphine increased the serum prolactin (PRL) levels of male Wistar rats in a dose dependent manner. This effect was abolished by naloxone and apomorphine, but not by diphenhydramine. Haloperidol also increased serum PRL, and this effect

was abolished by apomorphine but not by naloxone. Repeated administration of increasing doses of morphine attentuated the response of serum PRL to morphine. Naloxone did not alter the serum PRL levels of morphine tolerant rats. Neither haloperidol nor morphine increased the release of PRL from the isolated anterior pituitary. However, haloperidol (but not morphine) reversed the inhibition by dopamine of the in vitro release of pituitary PRL. 19 references. (Author abstract modified)

002221 Neal, M. J.; Bowery, N. G. Department of Pharmacology, School of Pharmacy, University of London, London WC1N 1AX, England **Differential effects of veratridine and potassium depolarization on neuronal and glial GABA release.** Brain Research (Amsterdam). 167(2):337-343, 1979.

The effects of veratridine and potassium depolarizations on the release of tritiated gamma-aminobutyric acid (GABA) from neural tissues in which GABA uptake is neuronal (rat cerebrocortical slices and frog retina) or glial (rat retina, spinal, and sympathetic ganglia) were studied. The neuronal but not the glial release of (3H)GABA was greatly increased by potassium chloride (KCl, 25mM) and veratridine (10mcM). The neuronal release of (3H)GABA evoked with KCl was calcium dependent, but the small KCl-induced increases in glial release were not reduced in the absence of calcium, even when magnesium ions were included in the medium. The veratridine-induced release of (3H)GABA from cortical slices was greatly potentiated in calcium-free medium, but the veratridine-induced release of tritiated noradrenaline was calcium dependent. The insensitivity of the glial GABA release mechanism to potassium depolarization suggests that the release of endogenous GABA from glial pools to response to physiological increases in extracellular potassium is not likely to be important. 20 references. (Author abstract modified)

002222 Nestoros, J. N.; Nistri, A. Dept. of Research in Anaesthesia, McGill University, 3655 Drummond Street, Montreal, Quebec Canada H3G 1Y6 **A presynaptic component of the action of iontophoretically applied flurazepam on feline cortical neurones.** Canadian Journal of Physiology and Pharmacology (Ottawa). 56(5):889-892, 1978.

The effect of iontophoretically applied flurazepam on the spike activity of pericruciate cortical neurons of the cat was studied. Flurazepam increased cortical inhibition produced either by local electrical stimulation (which is known to release gamma-aminobutyric acid (GABA)) or by iontophoretically applied GABA. Following intravenous treatment with thiosemicarbazide (a GABA synthesis inhibitor), flurazepam still augmented the action of GABA but was much less effective on electrically evoked cortical inhibition. These findings suggest that part of the action of flurazepam on inhibitory cortical transmission might be at the presynaptic level. 19 references. (Author abstract)

002223 Nicolau, Mauro; Lapa, A. J.; Valle, J. R. Dept. Ciencias Fisiologicas, Faculdade de Medicina de Marilia, Caixa Postal 451, 17500 Marilia, SP, Brazil **The inhibitory effects induced by delta9-tetrahydrocannabinol on the contractions of the isolated rat vas deferens.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 236(1):131-136, 1978.

The influence of delta9-tetrahydrocannabinol (THC) on the contractions of the isolated rat vas deferens induced by sympathomimetic, parasympathomimetic, and direct spasmogenic drugs was examined. THC exerted a noncompetitive inhibition of noradrenaline and of acetylcholine responses, but no synergistic action nor competitive antagonism was seen on the dose range used. It is concluded that the effects induced by THC added to in vitro preparations are not completely understood; they are dependent on the animal chosen, the organ used, the doses added to the nutritive solution, and the duration of the drug interaction. 13 references. (Author abstract modified)

002224 Nicoll, R. A. Dept. of Pharmacology and Physiology, University of California, San Francisco, CA 94143 **Pentobarbital: differential postsynaptic actions on sympathetic ganglion cells.** Science. 199(4327):451-452, 1978.

The frog sympathetic ganglion was used to elucidate the cellular mechanism of barbiturate anesthesia. Anesthetic concentrations of pentobarbital markedly reduced the fast nicotinic excitatory postsynaptic potential while having no effect on the slow excitatory postsynaptic potential or slow inhibitory postsynaptic potential, even though all three synaptic potentials depend on the presynaptic release of acetylcholine. A similar differential effect was seen for nicotinic and muscarinic responses to exogenously applied agonists, while the depolarizing action of gamma aminobutyric acid (GABA) was enhanced. These results indicate that pentobarbital has remarkably selective actions on the sympathetic ganglion and further indicate that blockade of ganglionic transmission by anesthetic concentrations of pentobarbital can be entirely explained by a postsynaptic action. Results strengthen the concept that pentobarbital anesthesia results from a postsynaptic blockade of central excitatory synapses which increase sodium conductance coupled with a post synaptic enhancement of GABA mediated synaptic inhibition. 18 references. (Author abstract)

002225 Nomura, Yasuyuki; Tanaka, Yasue; Segawa, Tomio. Dept. of Pharmacology, Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine, Kasumi 1-2-3, Hiroshima 734, Japan **Influences of sodium, ouabain and tricyclic antidepressant drugs on L-(3H)norepinephrine uptake into synaptosomal fractions of developing rat brain.** Japanese Journal of Pharmacology (Kyoto). 28(3):501-504, 1978.

To investigate the sodium dependence and specificity of the high affinity L-(3H)norepinephrine (L-(3H)NE) transport mechanism in the neonatal brain, the influence of sodium, ouabain, desmethylimipramine (DMI) and imipramine (IM) on the L-(3H)NE uptake into synaptosomal fractions of the developing rat brain were studied. Active L-(3H)NE uptake was lower in the neonate than in the adult, and ouabain inhibited the active uptake more strongly in the adult than in the neonate. It is suggested that the terminals do not acquire much sodium when the external sodium is low, even though the sodium pump is inhibited. Fifteen mM sodium was effective in activating the NE transport system, but the effect of 133 mM sodium was significantly stronger at both stages. Since a kinetic study on L-(3H)NE uptake into neonatal synaptosomal fractions showed the same value of Km as seen in adult synaptosomal fractions at lower concentrations of L-(3H)NE in suspending medium, it is concluded that neonatal synaptosomes already have a sodium dependent, high affinity L-(3H)NE uptake system. 13 references.

002226 Ogle, C. W.; Cho, C. H. Department of Pharmacology, Faculty of Medicine, University of Hong Kong, Hong Kong **Protection by zinc sulphate against reserpine-induced ulceration and other gastric effects in the rat.** Pharmacology (Basel). 17(5):254-261, 1978.

The effects of intraperitoneal pretreatment, 48h beforehand, with zinc sulfate (22, 44, or 88mg/kg) on gastric ulceration, gastric secretion, and changes in stomach wall mast cell counts induced after 4h by reserpine (5mg/kg) given intraperitoneally to intact (unoperated for pylorus occlusion) or pylorus occluded rats were examined. Zinc sulfate dose dependently antagonized the gastric actions of reserpine by preventing ulceration in the ruminal and glandular segments of the stomach, reducing acid

secretion, and inhibiting mast cell degranulation which occurred mainly in the glandular mucosal layer. The relationship between these findings and the action of zinc on gastric mast cells is discussed. 23 references. (Author abstract)

002227 Oishi, Ryozo; Suenaga, Noriko; Fukuda, Takeo. Department of Pharmacology, Faculty of Medicine, Kyushu University 60, Fukuo 812, Japan **Possible involvement of brainstem norepinephrine in pentylenetetrazol convulsions in rats.** Pharmacology Biochemistry and Behavior. 10(1):57-61, 1979.

The thresholds for twitch and clonic convulsion induced by intravenous infusion of pentylenetetrazol (PTZ) were measured in male Wistar King A rats treated with 6-hydroxydopamine (6-OHDA). In adult rats, intraventricular administration of 6-OHDA increased susceptibility to PTZ convulsions and decreased norepinephrine (NE) contents of the cortex, hypothalamus, and brainstem. When 6-OHDA was applied intraventricularly 8 days after birth, adult PTZ convulsion susceptibility was slightly decreased and brainstem NE content was significantly increased. The effects of 6-OHDA given 20 days after birth were similar to those seen in adults. Significant decreases in cortical and hypothalamic NE contents, with no change in PTZ convulsion susceptibility, were seen after 6-OHDA injections into the dorsal and ventral NE bundles. Results suggest that the brainstem NE neurons play an inhibitory role in the development of PTZ convulsions. 32 references. (Author abstract modified)

002228 Olpe, Hans-Rudolf; Koella, Werner P. Research Department, Pharmaceuticals Division, Ciba-Geigy Ltd., Basle, Switzerland **Inhibition of nigral and neocortical cells by gamma-hydroxybutyrate: a microiontophoretic investigation.** European Journal of Pharmacology (Amsterdam). 53(4):359-364, 1979.

Gamma-hydroxybutyrate (GHB) and gamma-aminobutyrate (GABA) were applied microiontophoretically near spontaneously active cells in the substantia nigra and neocortex of male Sprague-Dawley rats anesthetized with chloral hydrate. At low doses (20nA ejection currents), GABA depressed the activity of cells in both areas. GHB reduced the firing rate only when the compound was expelled with two to three times higher ejection currents; under these conditions, GHB depressed about half the nigral cells and the majority of the neocortical cells tested. The depressant action of GABA was readily antagonized by microiontophoretic bicuculline methiodide, but the effects of GHB were resistant to this alkaloid. Intraperitoneally administrated GHB (300 and 600mg/kg) reduced the firing rate of the majority of spontaneously active neocortical cells. It is concluded that GHB inhibits the firing of nigral and neocortical neurons, but that its effects are not mediated through the activation of bicuculline sensitive GABA receptors. 20 references. (Author abstract modified)

002229 Opmeer, Fred A.; Van Ree, Jan M. Rudolf Magnus Institute of Pharmacology, Medical Faculty, University of Utrecht, Vondellaan 6, Utrecht, The Netherlands **Competitive antagonism of morphine action in vitro by calcium.** European Journal of Pharmacology (Amsterdam). 53(4):395-397, 1979.

The influence of calcium on the inhibitory effect of morphine on the electrically-induced contractions of the guinea-pig ileum preparation was investigated in vitro. Results indicate that calcium ions diminish the response to morphine in a dose dependent manner, with the highest concentration of calcium ions completely reversing the morphine effect. Analysis of the data according to a Lineweaver-Burk transformation indicates that the interaction of calcium ions and morphine resemble competitive antagonism. The mechanism underlying this competitive antagonism is not clear; it is suggested that morphine alters calcium ion disposition, resulting in reduced neurotransmitter release. 5 references. (Author abstract modified)

002230 Osborne, Neville N.; Sontag, Karl-H. Forschungsstelle Neurochemie, Max Planck Institute, Gottingen, Germany **Some characteristics of mutant Han-Wistar rats which exhibit paresis and paralysis.** Advances in Biochemical Psychopharmacology. 19:357-361, 1978.

Electrophysiological and biochemical studies were performed in mutant Han-Wistar rats with spastic paresis and partial paralysis to determine their suitability as models for the study of Parkinson's disease. The activity of tyrosine hydroxylase in the striata of the mutant rats was significantly decreased, relative to controls, as it is in Parkinson's disease. However, the dopamine content in the mutant striata was significantly greater than in controls, whereas Parkinson's disease is characterized by diminished striatal dopamine content. Choline acetyltransferase activity was greatly enhanced in the mutant striata, whereas Parkinson's patients have almost normal enzyme activity. It is concluded that the balance between cholinergic, dopaminergic, and gamma-aminobutyric acid containing neurons in the nigro/basal ganglia/nigral loop in the mutant rats is fundamentally different from that in controls and in patients with Parkinson's disease. 8 references.

002231 Pagnini, Giuseppe; Camanni, Franco; Crispino, Antonio; Portaleone, Paolo. Institute of Pharmacology, University of Turin, C.so Raffaello 30, Turin, Italy **Effects of bromocriptine on adenylate cyclase and phosphodiesterase activities of rat striatum.** Journal of Pharmacy and Pharmacology (London). 30(2):92-95, 1978.

The activity of 2-bromo-alpha-ergokryptine (bromocriptine) on adenylate cyclase activity and on phosphodiesterase (PDE I and PDE II) activities in the rat striatum was investigated. Both in vivo and in vitro, bromocriptine stimulated adenylate cyclase activity, but reduced the stimulating effect of dopamine (DA) on adenylate cyclase activity. In vitro, bromocriptine showed a dose dependent biphasic action on the phosphodiesterases, with activation being produced at low concentrations and inhibition being produced at high concentrations. In vivo, bromocriptine stimulated both phosphodiesterases. It is posited that bromocriptine has an agonist/antagonist action at the striatal DA receptor level, with a relevant effect on the cyclic 3',5'-adenosine monophosphate system. 25 references. (Author abstract modified)

002232 Pajunen, A. E. I.; Hietala, Oili A.; Baruch-Virransalo, Eeva-Liisa; Piha, R. S. Department of Biochemistry, University of Oulu, SF-90100 Oulu 10, Finland **The effect of DL-allylglycine on polyamine and GABA metabolism in mouse brain.** Journal of Neurochemistry (Oxford). 32(5):1401-1408, 1979.

Intraperitoneal administration of the glutamate decarboxylase inhibitor DL-allylglycine caused a marked decrease in male NMRI mouse brain gamma-aminobutyric acid (GABA) concentration, a dramatic increase in L-ornithine decarboxylase activity, and a decrease in S-adenosyl-L-methionine, followed by putrescine accumulation. The treatment did not alter the degree of GABA formation from putrescine, however. The timing of the recovery of glutamate decarboxylase activity after the injection of DL-allylglycine was concomitant with that of the GABA concentration, suggesting that glutamate decarboxylase may be solely responsible for making up the GABA deficit caused by DL-allylglycine and that changes in polyamine metabolism are associated in some indirect way with the recovery process. 41 references. (Author abstract modified)

002233 Palmer, Gene C.; Jones, David J.; Medina, Miguel A.; Palmer, S. Jo; Stavinoha, William B. Department of Pharmacology, College of Medicine, University of South Alabama, 307

University Blvd., Mobile, AL 36688 **Role of neuroleptic agents on mouse pulmonary cyclic nucleotide systems.** Pharmacology (Basel). 17(5):280-287, 1978.

In a demonstration of the role of neuroleptic agents on mouse pulmonary cyclic nucleotide systems, the norepinephrine (NE) induced accumulation of cyclic adenosine monophosphate (AMP) in incubated tissue slices of mouse lung was inhibited by chloropromazine (CPZ) and to a lesser extent by haloperidol. In particulate lung fractions, both agents blocked dopamine sensitive adenylate cyclase to a greater degree than the NE responsive enzyme. Again, CPZ was more potent than haloperidol. Acute injections (1/2 - 8h) of the neuroleptics usually resulted in lower steady-state levels of pulmonary cyclic AMP and cyclic guanosine monophosphate (GMP) following rapid (0.5sec) tissue inactivation by microwave irradiation. On a subchronic injection schedule, the in vivo levels of pulmonary cyclic AMP tended to increase. 25 references. (Author abstract modified)

002234 Paul, Steven M.; Skolnick, Phil. Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, MD 20014 **Rapid changes in brain benzodiazepine receptors after experimental seizures.** Science. 202(4370):892-894, 1978.

The effect of experimentally induced (electroshock or injection of pentylenetetrazol) on binding of labeled diazepam was examined in adult male Sprague-Dawley rats. Both chemically and electrically-induced seizures increased specific binding of diazepam to putative receptor sites in cerebral cortical membrances. Nonspecific binding was not significantly affected by any of the experimental conditions, nor were changes due secondary seizure induced hypoxia. The enhancement of diazepam binding resulted from a rapid increase in the number of available binding sites, rather than a change in receptor affinity. The postictal increase in cortical benzodiazepine receptors suggests that the cerebral cortex might be more sensitive to the anticonvulsant effects of the benzodiazepines after seizures. This may be related to the mechanism of action of these drugs in the treatment of recurrent seizures such as status epilepticus. 17 references. (Author abstract modified)

002235 Paul, Von A.; Mildner, B.; Chandra, P. Chandra: Gustav-Emden-Zentrum der Biolog. Chemie, Abteilung fur Molekularbiologie, Theodor-Stern-Kai 7, D-6000 Frankfurt/Main 70, Germany /**Influence of metergoline on the biosynthesis of brain macromolecules.**/ Beeinflussung der Biosynthese von Makromolekulen im Gehirn durch Metergolin. Arzneimittel-Forschung (Aulendorf). 28(l):25-29, 1978.

The influence of metergoline on cellular protein synthesis in the mouse brain was studied in vivo, after intraperitoneal administration of 50mcg doses. Brain samples analyzed at different intervals after drug treatment showed a short-term increase of 3H-leucine incorporation into proteins, followed by a gradual decline of level. The latter reached control level about 18 hours after the drug administration. Under similar experimental treatments, metergoline had no effect on the biosynthesis of ribonucleic acid (RNA) catalyzed by magnesium ions; however, a slight stimulation of manganese activated RNA biosynthesis by the drug was seen. Mice receiving intraperitoneal injections of 50mcg of metergoline showed increased brain methyltransferase activity; the maximum stimulation was observed one hour after drug treatment. In another set of experiments, the ability of mouse brain preparations to catalyze the methyl group incorporation in the exogenously added transfer RNA (tRNA) was found to decrease with increasing age of the animals; the addition of metergoline to the incubation medium enhanced endogenous methylation, especially in the older animals. On the contrary, the ability to methylate the exogenously added heterologous tRNA was not affected by metergoline, irrespective of the age of the animals. Preliminary data from experiments on the effect of this drug on conditioned learning in rats indicate that the drug is able to enhance the learning ratios. 22 references. (Journal abstract modified)

002236 Pearl, Ronald G.; Seiden, Lewis S. Dept. of Pharmacological and Physiological Sciences, University of Chicago, 947 East 58th Street, Chicago, IL 60637 **d-Amphetamine-induced increase in catecholamine synthesis in the corpus striatum of the rat: persistence of the effect after tolerance. (Unpublished paper).** Research Report, NIMH Grant MH-11191, 1978. 31 p.

The effect of d-amphetamine on in vivo catecholamine synthesis in four regions of rat brain was determined by measuring the accumulation of dopa after inhibition of dopa decarboxylase. In doses up to 2.5mg/kg, d-amphetamine caused dose dependent increases in striatal dopa accumulation to a maximum of 280% of control; further increase in dose resulted in smaller effects until 10mg/kg d-amphetamine was not significantly different from control. Results suggest that tolerance to d-amphetamine is not related to its effect on catecholamine synthesis but instead occurs via changes in aspects of catecholamine metabolism other than synthesis via change in catecholamine release, reuptake, or receptor sensitivity, or via changes in noncatecholaminergic mechanisms. 59 references. (Author abstract modified)

002237 Perry, Thomas L.; Hansen, Shirley; Kish, Stephen J. Department of Pharmacology, University of British Columbia, Vancouver, British Columbia, Canada V6T 1W5 **Effects of chronic administration of antipsychotic drugs on GABA and other amino acids in the mesolimbic area of rat brain.** Life Sciences (Oxford). 24(3):283-288, 1979.

Female Wistar rats were injected once daily with chlorpromazine (20mg/kg) or haloperidol (3mg/kg) for 100 days and were sacrificed 24 hours or 35 days after the last injection. Brains were frozen rapidly in liquid nitrogen, and the mesolimbic area and striatum were dissected from each frozen brain. Amino acids were quantitated in the mesolimbic area and glutamic acid decarboxylase (GAD) activity was measured in the striatum. Chronic administration of chlorpromazine and haloperidol did not alter brain gamma-aminobutyric acid (GABA) content or GAD activity in the treated rats, compared to controls. However, a significant elevation of aspartate content and a reduction of glycine content was found after chronic administration of haloperidol. Results indicate that alterations found in the GABA system of autopsied brain from psychotic patients do not result from previous antipsychotic drug therapy. 21 references. (Author abstract modified)

002238 Petrali-Cicognara, Elena Harriet. University of Saskatchewan, Canada **The uptake and release of some monoamines in the rat brain. (Ph.D. dissertation).** Disseration Abstracts International. 39(5):2158-B, 1978. (Not available from University Microfilms), 1977.

The uptake and release of trace amines, from rat brain tissue, was studied in four experiments. In Experiment 1, the autoradiographic distribution of radioactively labeled beta-phenylethylamine, tryptamine, octopamine, noradrenaline, serotinin, dopamine, DOPA, p-tyramine, tyrosine, and inulin, following their intraventricular injection, was studied. Results show that distribution of these amines is limited to an area adjacent to ventricle and subarachnoid space. In Experiment 2, further studies on uptake and release of p-tyramine and dopamine were conducted using slices prepared from the hypothalamus and caudate maintained in vitro. Results indicate that both amines exhibit a high and low affinity uptake system in both brain regions studied. In

Experiment 3, tests conducted with desieramine and benxtropine indicate that desipramine is 14 times more effective in blocking p-tyramine than dopamine uptake in the hypothalamus. Benztropine is equally effective in blocking p-tyramine and dopamine uptake in the hypothalamus but nine times more effective as a dopamine blocker in the caudate. In Experiment 4, tests in which the substantia nigra was lesioned indicate a correspondence between reduction in uptake velocity and endogenous dopamine levels only in the case of dopamine in the high affinity substrate concentration range. Results suggest that p-tyramine high affinity uptake is not dependent on the presence of dopamine neurones. (Journal abstract modified)

002239 Piercey, Montford F.; Hollister, Rusel P. Upjohn Company, CNS Research, Kalamazoo, MI 49001 **Effects of intravenous baclofen on dorsal horn neurons of spinal cats.** European Journal of Pharmacology (Amsterdam). 53(4):379-382, 1979.

Baclofen (1mg/kg iv) abolished or severely attenuated the high threshold late component, but not the low threshold early component, of long duration (greater than 150msec) discharges evoked in cat dorsal horn neurons by intense transcutaneous electrical stimulation. Baclofen similarly reduced the spontaneous activities and discharges evoked by intraarterial bradykinin in these same cells. These powerful inhibitions of dorsal horn interneurons may be the basis of the reported analgesic actions of baclofen and may contribute to depression in reflex excitability of motoneurons. 12 references. (Author abstract modified)

002240 Pilotte, Nancy Saplikoski. Florida State University **Onset of puberty and sexual behavior in female rats after neonatal modification of monoaminergic neurotransmitters. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 7801506, HC$15. MF$7.50. 70 p. 1977.

Neonatal female rats were treated with one of the neurotransmitter precursors 5-hydroxytrypotophan (5-HTP), 1-3,4-dihydroxyphenylalanine (DOPA), or 1-3,4-dihydroxyphenylserine (DOPS) to assess the early actions of serotonin, dopamine and norepinephrine on the development and maintenance of the reproductive processes. Rats were also treated with the monoamine depletor reserpine, alone or in combination with one of the precursors on postnatal days 2, 5 or 2 and 5. Results indicated that temporary monoamine modification in the early postnatal period can have lasting effects on the reproductive processes and that the sexual maturation of the female rat may be related to the concentrations of central monoamines during the neonatal period. Vaginal opening was earlier in rats given 5-HTP on day 2 or DOPA or DOPS on day 5, or DOPA on days 2 and 5, or the combination of reserpine on day 2 and DOPS on day 5 than in saline controls. Early treatment with the monoaminergic modifiers also affected adult lordotic behavior. Results indicate that 1) temporary monoamine modification in the early postnatal period can have lasting effects on the reproductive processes of the rat, and 2) sexual maturation of the female rat may be related to the concentration of central monoamines during the neonatal period. (Journal abstract modified)

002241 Piris, P.; Beaughard, M.; Cosnier, D.; Labrid, C. Dept. of Pharmacology, CERM, F-203 Riom Cedex, France **Activity of bepridil and other anti-anginals on cardiovascular modifications engendered by conditioned anxiety in the dog.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 235(1):147-164, 1978.

The effects of bepridil (5mg/kg i.v.), perhexilene (5mg/kg), propranolol (0.5mg/kg), dipyridamole (0.5mg/kg), amiodarone (10mg/kg), pentaerythritol tetranitrate (40mcg/kg), and nitroglycerine (40mcg//kg) on cardiovascular manifestations of auditory-induced emotional stress were examined in conscious mongrel dogs of both sexes. Bepridil, perhexilene, and propranolol considerably reduced tachycardia provoked by the anxiogenic stimulus; nitroglycerin exerted was less potent in this respect, and the remaining drugs had no effect. Bepridil, nitroglycerin, perhexilene, propranolol, and pentaeryhthritol all significantly reduced the elevation of the Robinson index, whereas amiodarone and dipyradamole were without effect. None of the drugs significantly reduced systolic hypertension associated with the induction of conditioned anxiety. 42 references. (Author abstract modified)

002242 Pirogov, A. A.; Orlov, A. A.; Vorob'yeva, I. S. Kafedra fiziologii vysshey nervnoy deyatel'nosti Leningradskogo gosudarstvennogo universiteta, Leningrad, USSR /**The influence of aminazine on the functional state of the feline sensorimotor cortex.**/ Vliyaniye aminazina na funktsional'noye sostoyaniye sensomotornoy kory koshki. Fiziologicheskiy Zhurnal SSSR imeni I. M. Sechenova (Leningrad). 64(8):1066-1073, 1978.

Twenty full grown cats were anesthetized and fitted with stimulating and registering electrodes in order to study the effect of aminazine on the sensorimotor cortex under severe surgical conditions, including artificial breathing. The aminazine was introduced both intravenously and directly into the reticular formation. The administration of aminazine was found to shorten by 150 to 300 msec the recovery cycles of evoked responses or responses of the individual neurons of the sensorimotor cortex to monosensory stimulation or stimulation of the pyramidal tract at the level of the cortex or cerebral peduncles. The cortical evoked responses displayed a degree of habituation over time to the aminazine doses. 15 references. (Journal abstract modified)

002243 Propst, Friedrich; Moroder, Luis; Wunsch, Erich; Hamprecht, Bernd. Max-Planck-Institut fur Biochemie, D-8033 Martinsried, Germany **The influence of secretin, glucagon and other peptides, of amino acids, prostaglandin endoperoxide analogues and diazepam on the level of adenosine 3',5'-cyclic monophosphate in neuroblastoma x glioma hybrid cells.** Journal of Neurochemistry (Oxford). 32(5):1495-1500, 1979.

The effects of a series of compounds (including diazepam, amino acids, endoperoxide analogues, secretin, glucagon, and other peptides and peptide hormones) on the level of adenosine 3',5'-cyclic monophosphate (cyclic AMP) in neuroblastoma/glioma hybrid cells were studied. Two prostaglandin endoperoxide analogues exhibited weak stimulatory action when applied in micromolar or larger concentrations. At nanomolar concentrations, only the gastrointestinal hormones secretin and glucagon stimulated the formation of cyclic AMP, as detected in the presence of a phosphodiesterase inhibitor. The effect of secretin but not of glucagon was antagonized by secretin-(5-17), suggesting that secretin and glucagon act on the cells via different receptors. 43 references. (Author abstract modified)

002244 Pugsley, T. A.; Lippmann, W. Biochemical Pharmacology Department, Ayerst Laboratories, P. O. Box 6115, Montreal, Quebec, Canada H3C 3J1 **Effect of metiamide, a histamine H2-receptor antagonist on the clonidine-induced decrease in rat brain noradrenaline turnover.** Journal of Pharmacy and Pharmacology (London). 31(1):51-52, 1979.

The effects of the histamine H2 receptor antagonist metiamide and the alpha-adrenergic agonist clonidine on the turnover of noradrenaline in male Sprague-Dawley rat brain were examined. Clonidine reduced the depletion of brain noradrenaline following inhibition of noradrenaline synthesis by the dopamine-beta-hydroxylase inhibitor bis-(4-methyl-1-homopiperazinyl-thiocarbonyl) disulfide, indicating a reduction in noradrenaline turn-

over. Metiamide did not affect noradrenaline turnover or the clonidine-induced reduction in brain adrenaline turnover. Results indicate that the decrease in catecholamine turnover induced by clonidine is independent of any direct effect of clonidine on H2receptors. 20 references.

002245 Pugsley, T. A.; Lippmann, W. Biochemical Pharmacology Department, Ayerst Laboratories, P. O. Box 6115, Montreal, Quebec, Canada H3C 3JI **Effects of chlorine substituents on the benzene rings of an analogue of the antipsychotic drug butaclamol on the interaction with dopamine and muscarinic receptors in rat brain.** Journal of Pharmacy and Pharmacology (London). 31(1):47-49, 1979.

The effects of chlorine substituents on the benzene rings of the butaclamol analogue dexclamol hydrochloride or (●)-5 on its interaction with dopamine and muscarinic receptors in male Sprague-Dawley rat brain were examined. Results indicate that introduction of a chlorine substituent at various positions of the ring system of (●)-5 decreases the in vitro and in vivo potencies of the compound toward dopamine related mechanisms. HF-2046, the cis-isomer of the neuroleptic clozapine, which differs from clozapine only in the position of the chlorine substituent relative to the piperazinyl side chain, displayed a profile of a typical cataleptic neuroleptic agent, whereas clozapine is a non-cataleptic neuroleptic. 23 references.

002246 Quik, M.; Emson, P. C.; Joyce, E. Department of Pharmacology and Therapeutics, McGill University, 3655 Drummond St., Montreal, Quebec H3G 1Y6, Canada **Dissociation between the presynaptic dopamine-sensitive adenylate cyclase and (3H)spiperone binding sites in rat substantia nigra.** Brain Research (Amsterdam). 167(2):355-365, 1979.

Tritiated spiperone binding sites and dopamine (DA) sensitive adenylate cyclase activity were measured in male Sprague-Dawley rat substantia nigra (s. nigra) 7 or 14 days after various lesions. Hemisections, which resulted in a 66% decline in tyrosine hydroxylase and in cyclic nucleotide phosphodiesterase and a 73% decline in glutamate decarboxylase, led to a 50% decrease in (3H)spiperone binding and to the almost complete disappearance of DA sensitive adenylate cyclase from the s. nigra on the lesioned site. Nigral injections of 6-hydroxydopamine reduced tyrosine hydroxylase activity in the nigra by 85% and (3H)spiperone binding by 40%, but had no effects on phosphodiesterase or DA sensitive adenylate cyclase activity. Intrastriatal injections of kainic acid did not alter tyrosine hydroxylase activity in the s. nigra, but decreased both glutamate decarboxylase (54%) and phosphodiesterase (68%); (3H)spiperone binding was unaffected by this lesion, but DA sensitive adenylate cyclase was greatly reduced (50-75%). Results suggest that DA receptor binding sites in the s. nigra are located on DA neurons, while DA sensitive adenylate cyclase is located presynaptically on striatonigral nerve terminals. 41 references. (Author abstract modified)

002247 Raisman, R.; Briley, M.; Langer, S. Z. Synthelabo, LERS, Department of Biology, 58 rue de la Glaciere, F-75013 Paris, France **High-affinity 3H-imipramine binding in rat cerebral cortex.** European Journal of Pharmacology (Amsterdam). 54(3):307-308, 1979.

The presence of specific high affinity binding sites for tritiated imipramine in male Sprague-Dawley rat cerebral cortex was demonstrated. The specific binding of 3H-imipramine was saturable, giving a linear Scatchard plot indicative of a single population of binding sites. The apparent dissociation constant was 6.8nM, with a maximal binding capacity of 22.7pmole/g tissue. The specific binding of 3H-imipramine was displaced by low concentrations of other tricyclic antidepressants such as amitriptyline, desipramine, and chlorimipramine; a typical antidepressants such as iprindol and mianserine displaced binding at much higher concentrations. Noradrenaline displaced less than 30% binding at 100 mcM, whereas serotonin displaced 50% at 1mcM. The specificity of high affinity 3H-imipramine binding does not appear to be identical to that of any receptor so far studied. Since chronic treatment with desipramine results in a substantial decrease in 3H-imipramine binding in rat cerebral cortex, the study of high affinity 3H-imipramine binding may offer a new approach to the study of depression and the search for new antidepressant drugs. 5 references.

002248 Rastogi, R. B.; Lapierre, Y. D.; Singhal, R. L. Bio-Research Laboratories, Connlab Holdings Limited, 265 Hymus Boulevard, Pointe Claire, Montreal, Quebec, Canada **Synaptosomal uptake of norepinephrine and 5-hydroxytryptamine and synthesis of catecholamines during benzodiazepine treatment.** Canadian Journal of Physiology and Pharmacology (Ottawa). 56(5):777-784, 1978.

The synaptosomal uptake of norepinephrine (NE) and 5-hydroxytryptamine (5-HT) and synthesis of catecholamines during benzodiazepine treatment were investigated in rats. Administration of diazepam acutely or for 22 consecutive days decreased spontaneous locomotor activity and presumably the release of NE and DA as evidenced by increased levels of these amines in crude synaptosomes and low levels of their metabolites, 4-hydroxy-3-methoxyphenylglycol in brain and homovanillic acid (HVA) in striatum of rats. Acute or chronic diazepam elevated the levels of synaptosomal 5-HT by 21% and 50%, respectively, suggesting that the release of this indoleamine was also diminished. Withdrawal of rats from diazepam decreased the rate of synthesis of 5-HT and the level of 5-HT within the crude synaptosomes; the latter could be attributed to enhanced release and impeded uptake of this indoleamine. The view gains support from enhanced levels of the metabolite 5-hydroxyindoleacetic acid seen in several brain areas of withdrawn rats. The data suggest that diazepam exerts its central effects on mood and behavior by impairing the release of catecholamines and 5-HT. It is also suggested that enhanced release and decreased uptake of these monoamines may, in part, be responsible for the hyperexcitability seen during the rebound phase in anxious patients withdrawn from benzodiazepine therapy. 34 references. (Author abstract modified)

002249 Reubi, J.-C.; Iversen, L. L.; Jessell, T. M. MRC Neurochemical Pharmacology Unit, Department of Pharmacology, Medical School, Cambridge, England **Regulation of GABA release by dopamine in the rat substantia nigra.** Advances in Biochemical Psychopharmacology. 19:401-404, 1978.

The effects of dopamine on the release of substance-P and gamma-aminobutyric acid (GABA) from superfused slices of rat substantia nigra were examined. Dopamine enhanced the spontaneous (but not potassium induced) release of GABA from the substanita nigra but had no significant effect on GABA release in the corpus striatum or hippocampus. Amphetamine also stimulated the release of GABA from the substantia nigra, suggesting that the release of endogenous dopamine from the dendrites of the substantia nigra can stimulate a local release of GABA. Dopamine did not affect the spontaneous or potassium evoked release of substance-P, suggesting that dopamine receptors are located predominantly on GABA containing striatonigral terminals. The implications of these findings for the local feedback inhibition of dopaminergic neurons within the substantia nigra are discussed. 6 references.

002250 Richert, John R.; Driscoll, Bernard F.; Kies, Marian W.; Alvord, Ellsworth C., Jr. Section on Myelin Chemistry, Laboratory of Cerebral Metabolism, NIMH, Bethesda, MD

20014 **Adoptive transfer of experimental allergic encephalomyelitis: incubation of rat spleen cells with specific antigen. (Unpublished paper).** Bethesda, MD, NIMH, 1978. 17 p.

Observations on transfer of experimental allergic encephalomyelitis (EAE) in the Lewis rat were extended to include spleen cells incubated with guinea-pig specific antigen, myelin basic protein. Spleen cells from sensitized donor rats appear to be incapable of adoptively transferring EAE directly to normal recipients. It was found that incubation with specific antigen, myelin basic protein, permits transfer of EAE with spleen cells. Data are presented in which activation of EAE spleen cells by Concanavalin-A (Con-A) is compared with activation by myelin basic protein. The results suggest that Con-A and myelin basic protein may be acting through different mechanisms in their activation of spleen cells from sensitized donors. Cellular proliferation does not appear to be necessary for in vitro activation with specific antigen. 10 references. (Author abstract modified)

002251 Richter, Judith A. Dept. of Pharmacology, Indiana University School of Medicine, 1100 W. Michigan St., Indianapolis, IN 46202 **CNS tolerance to the hypnotic effect of pentobarbital in rats by injections of pentobarbital suspension.** Neuropharmacology (Oxford). 18(2):183-191, 1979.

Functional CNS tolerance to the hypnotic effect of barbiturates was determined in vivo by comparing the brain barbiturate level at awakening from a test dose in control male Wistar rats and in rats chronically treated with barbiturate. Administration of increasing concentrations of barbital in drinking water resulted in a twofold tolerance to barbital, which was lost after the 3 days of withdrawal necessary to eliminate the drug from the brain. No significant CNS tolerance to the hypnotic effect of pentobarbital was seen after administration in food or water on various schedules. However administration of pentobarbital by daily ip injections resulted in approximately 1.5times increase in CNS tolerance to the hypnotic effect of the drug in 5-10 days. Barbiturates in vitro inhibited potassium stimulated acetylcholine release from brain slices, and the degree of inhibition by pentobarbital in vitro was not altered by chronic ip injections of pentobarbital in vivo. 23 references. (Author abstract modified)

002252 Rivera-Calimlim, Leonor; Bosmann, H. Bruce; Penney, David P.; Karch, Fred E. Dept. of Pharmacology and Toxicology, University of Rochester School of Medicine and Dentistry, Rochester, NY **Biochemical, morphologic and physiologic changes in the adrenal glands of rats chronically treated with phenobarbital.** Research Communications in Chemical Pathology and Pharmacology. 21(1):1-14, 1978.

Biochemical and ultrastructural changes in the adrenal glands of rats were studied after long-term phenobarbital treatment. At the fine structural level, the parenchymal cells of the phenobarbital treated rats resembled cortical cells that had been stimulated by adrenocorticotropin. Very large hollow mitochondria characterized by loss of vesicles and cristae with retention of the double outer membrane were found. Arylesterase activity, the marker used for rough endoplasmic reticulum, was significantly diminished. The relative decrease in arylesterase activity was consistent with the morphologic adrenal coritcal hyperplasia. Trypsin-like enzyme activity was increased. The plasma corticosterone response to adrenocorticotropin injection was not significantly different in treated and control rats. The similarity of the observed mitochondrial changes to the reported mitochondrial cavitation in the adrenal glands of rats treated with aminoglutethimide is discussed. 25 references. (Author abstract modified)

002253 Roberts, P. J.; Anderson, Susan D. Department of Physiology, School of Biochemical and Physiological Sciences, University of Southampton, Southampton S09 2TU, England **Stimulatory effect of L-glutamate and related amino acids on (3H)dopamine release from rat striatum: an in vitro model for glutamate actions.** Journal of Neurochemistry (Oxford). 32(5):1539-1545, 1979.

The effects of L-glutamate and a number of structural analogues on the spontaneous release of tritiated dopamine (3H-DA) from slices of female Wistar rat brain were examined. Glutamate and other excitatory acid amino acids produced a marked stimulation of 3H-DA release that was calcium dependent and unaffected by procaine or tetrodotoxin. The glutamate stimulated release was abolished in kainate lesioned striatum. The action of glutamate was effectively antagonized by L-glutamate diethylester and 2-amino-phosphonobutyric acid, but only weakly antagonized by L-methionine-DL-sulfoximine. Other proposed amino acid antagonists were inactive. The probable site of the releasing action of L-glutamate on presynaptic sites on nigrostriatal DA terminals is discussed. 44 references. (Author abstract modified)

002254 Robinson, J. H.; Wang, S. C. Department of Pharmacology, Columbia University, College of Physicians and Surgeons, New York, NY 10032 **Unit activity of limbic system neurons: effects of morphine, diazepam and neuroleptic agents.** Brain Research (Amsterdam). 166(1):149-159, 1979.

The effects of morphine, diazepam, and three neuroleptic agents (chlorpromazine, perphenazine, and haloperidol) on neuronal firing rates were studied in the limbic system of immobilized cats. Parietal craniotomy was carried out under 1.5-4.0% halothane. Extracellular potentials from single cells in the cingulate gyrus, septum, and lateral hypothalamic areas were recorded using glass coated, platinum/iridium microelectrodes. In general, intravenous administration of morphine sulfate augmented the spontaneous firing rates of most of the neurons studied. In contrast, diazepam produced a marked attenuation of both spontaneous and morphine augmented firing rates. The neuroleptic agents had no significant or consistent effect on the morphine augmented firing rates of neurons in these limbic areas. Results indicate that the limbic system is involved in the behavioral excitement induced by morphine in cats and in the depressant effect of diazepam. The inability of the neuroleptic agents to antagonize the morphine augmented neuronal firing rates suggests that these agents act outside these limbic areas. 24 references. (Author abstract modified)

002255 Rohde, B. H.; Rea, M. A.; Simon, J. R.; McBride, W. J. Department of Psychiatry, Institute of Psychiatric Research, Indiana University School of Medicine, Indianapolis, IN 46202 **Effects of X-irradiation induced loss of cerebellar granule cells on the synaptosomal levels and the high affinity uptake of amino acids.** Journal of Neurochemistry (Oxford). 32(5):1431-1435, 1979.

Glutamate and aspartate levels were significantly lower (by 25% and 15%, respectively) in crude synaptosomal (P2) preparations obtained from the cerebella of male Long-Evans hooded rats in which the granule cell population was selectively reduced by X-irradiation than in control cerebella. Glycine, taurine, and gamma-aminobutyric acid (GABA) levels were not altered by the irradiation treatment. The uptake of tritiated L-glutamate and l-aspartate was reduced by about 20% by the irradiation treatment, whereas the uptake of tritiated GABA and taurine was unchanged. In a second study, the uptake of tritiated glutamate, aspartate, and GABA was significantly reduced (to 57%, 68%, and 59%, respectively, of control values) in P2 fractions from the cerebella of rats in which the population of granule, stellate, and basket cells was reduced by irradiation. Results suggest that glutamate may be the excitatory transmittor

released from granule cells and GABA the inhibitory transmitter released from basket cells. 24 references. (Author abstract modified)

002256 Rosenberg, Howard C.; Chiu, Ted H. Dept. of Pharmacology, Medical College of Ohio, Toledo, OH 43699 **Decreased 3H-diazepam binding is a specific response to chronic benzodiazepine treatment.** Life Sciences (Oxford). 24(9):803-807, 1979.

Specific tritiated diazepam binding was measured in male Sprague-Dawley rat cortex after 7-10 days of twice daily treatment with large doses of flurazepam or barbital. Observer ratings of drug response each day indicated that barbital treated rats showed ataxia equal to or greater than that seen in benzodiazepine treated animals. Flurazepam treatment caused a 16% decrease in maximal 3H-diazepam binding, but no change in binding affinity. Barbital treatment caused no change in binding affinity or in maximal binding. Results indicate that decreased diazepam binding is a specific response to prolonged receptor occupation and not part of a more generalized adaptation to chronic CNS depression. 21 references. (Author abstract modified)

002257 Ross, Svante B. Research and Development Laboratories, Astra Lakemedel AB, S-151 85 Sodertalje, Sweden **The central stimultory action of inhibitors of the dopamine uptake.** Life Sciences (Oxford). 24(2):159-168, 1979.

The accumulation of tritiated dopamine in cell free homogenates of male NMRI mouse forebrain was inhibited by amfonelic acid, mazindol, nomifensine, methylphenidate, and d-amphetamine. Reserpine potentiated the action of d-amphetamine (20 fold), but had only slight effects on the other compounds. All five compounds produced pronounced hypermotility in mice, but only d-amphetamine was active in reserpinized mice. The other four compounds antagonized the hyperactivity produced by d-amphetamine in the reserpinized mice. Results suggest that d-amphetamine causes hyperactivity be releasing dopamine, whereas the other compounds act by inhibiting reuptake of dopamine. 28 references. (Author abstract modified)

002258 Rotrosen, John; Traficante, Louis J.; Covner, Bruce; Basuk, Paul; Gershon, Samuel. Neuropsychopharmacology Research Unit, Department of Psychiatry, New York University Medical Center, 550 First Avenue, New York, NY 10016 **Effects of plant lectins on cation-activated brain ATPases.** Life Sciences (Oxford). 23(12):1241-1247, 1978.

The effects of concanavalin A (Con A) and wheat germ agglutinin (WGA) on cation activated ATPases in a crude homogenate of rat brain corpus striatum were examined. Con A enhanced the activity of Mg dependent-, and Ca activated ATPases, and inhibited (Na K)-ATPase activity. WGA enhanced Mg dependent ATPase activity, but did not alter the activity of the other two components. The specificity of these interactions was demonstrated by reversal with specific lectin interacting sugars. The possibility that these effects may be mediated by lectin binding to physiologic regulatory sites, as well as the possible role of these interactions in the etiopathology of schizophrenia, are discussed. 34 references. (Author abstract)

002259 Roufogalis, B. D.; Thornton, M.; Wade, D. N. Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, V6T 1W5, Canada **Comparative study of the dopamine-sensitive adenylate cyclase in the striatum and hypothalamus of rat brain.** Journal of Pharmacy and Pharmacology (London). 31(1):33-38, 1979.

The stimulation by dopamine of adenylate cyclase in homogenates of male Fullensdorff rat striatum was enhanced in the presence of 0.6-3mM adenosine triphosphate (ATP) and 10-100mcM guanosine triphosphate (GTP). The dopamine stimulation was attributed to its antagonism of inhibition of adenylate cyclase by GTP or higher concentrations of ATP. The stimulation was dependent on magnesium chloride and was maximal when the magnesium chloride concentration was at least twice that of ATP. ATP did not inhibit adenylate cyclase in homogenates of the ventral hypothalamus, but GTP significantly stimulated it. Dopamine stimulated the adenylate cyclase in the hypothalamus. This action was blocked by 10mcM chlorpromazine or 100mcM phentolamine, but not by 100mcM propranolol or by the 1-chloro analogue of chlorpromazine, which lacks neuroleptic activity. 39 references. (Author abstract modified)

002260 Saavedra, Juan M. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Adrenaline levels in brain stem nuclei and effects of a PNMT inhibitor on spontaneously hypertensive rats.** Brain Research (Amsterdam). 166(2):283-292, 1979.

The adrenaline content of specific brainstem areas was decreased in young (4-weeks-old) but not in adult (14-weeks-old) spontaneously hypertensive rats (SHR). Some of these areas also showed increased phenylethanolamine N-methyltransferase (PNMT) activity, indicating a possible enhance release or metabolism of adrenaline early in the development of hypertension. Dopamine and noradrenaline levels are nor altered in young or adult SHR. Administration of a PNMT inhibitor to adult SHR resulted in a decrease of the blood pressure to control levels. These results suggest that adrenergic mechanims participate in the development of genetic hypertension and that PNMT inhibitors may have value as hypotensive agents. 42 references. (Author abstract modified)

002261 Saavedra, Juan M.; Grobecker, Horst. Laboratory of Clinical Science, NIMH, Bldg. 10, Room 2D-47, Bethesda, MD 20014 **Central and peripheral catecholamines in experimental and genetic hypertension. (Unpublished paper).** Bethesda, MD, NIMH, 1978. 25 p.

Central and peripheral catecholamines in two animal modes of hypertension were investigated. In spontaneous hypertensive rats (SHR), brainstem adrenaline levels were decreased and phenylethanolamine N-methyl transferase (PNMT) activity was increased early in the development of hypertension. In the DOCA-Salt hypertensive animals, enhanced PNMT activity in some brainstem areas occurred early in the treatment and extended to other brainstem areas with prolonged treatment and higher blood pressure. PNMT inhibitors, when administered systematically, resulated in a normalization of the blood pressure in both models studied. Results suggest that the metabolism of central and peripheral catecholamine can be interrelated, that both systems play a role in the development of genetic and experimental hypertension, and that the blockade of adrenaline synthesis can be used as a tool to modify the hypertension of genetic or renal origin. 41 references. (Author abstract modified)

002262 Salvaterra, Paul M.; Foders, Renee M. Division of Neurosciences, City of Hope National Medical Center, 1500 East Duarte Road, Duarte, CA 91010 **(125I)2alpha-bungarotoxin and (3H)quinuclidinylbenzilate binding in central nervous systems of different species.** Journal of Neurochemistry (Oxford). 32(5):1509-1517, 1979.

Binding sites for (125I)diiodo alpha-bungarotoxin ((125I)2BuTx) and (3H)quinuclidinylbenzilate ((3H)QNB) were measured in postnuclear membrane fractions prepared from whole brains or brain regions of Drosophila melanogaster, Torpedo californica, Carassius auratus, Rana pipiens, Rana catesbeiana, Rattus norvegicus, Mus muscalus, Oryctolagus cuniculus, and Bos. All species and regions except Drosphila had 16-150 times more (3H)QNB binding sites than (125I)2BuTx bind-

ing sites. Brain regions with the highest levels of (125I)2BuTx binding were Drosophila heads (300fmol/mg), goldfish optic tectum (80fmol/mg), and rat and mouse hippocampus (30-40fmol/mg). The highest levels of (3H)QNB binding were seen in rat and mouse caudate (1.3-1.6pmol/mg). Lowest levels of (3H)QNB and (1251)2BuTx binding were seen in cerebellum. The utility of (125I)2BuTx and (3H)QNB binding as quantitative measures of nicotinic and muscarinic acetylcholine receptors in CNS is discussed. 44 references. (Author abstract modified)

002263 Saner, A.; Pletscher, A. Research Division, F. Hoffmann-La Roche & Co. Ltd., Basel, Switzerland **Enhancement of 5-hydroxytryptamine synthesis in brain by monoamine-depleting drugs.** Journal of Pharmacy and Pharmacology (London). 30(2):115-117, 1978.

The effects of reserpine and of a benzoquinolizine derivative with a short lasting reserpine-like action, Ro 4-1284, on serotonin (5-hydroxytryptamine, 5-HT) synthesis, 5-HT metabolism, and on the increases in the 5-HT precursor 5-hydroxytryptophan (5-HTP) induced by the cerebral decarboxylase inhibitor 3-hydroxybenzylhydrazine hydrochloride (NSD-1015) were investigated in rats. Both of the monoamine depleting drugs produced a decrease in cerebral 5-HT and an increase in 5-hydroxyindoleacetic acid (5-HIAA). The action of Ro 4-1284 was relatively short lasting (about 4 to 8 hr) whereas, that of reserpine was of long duration (greater than 16 hr). Both drugs enhanced the NSD-1015-induced rise in 5-HTP. In reserpine-treated rats, the duration of the enhancement of the 5-HTP rise was longer than that after Ro 4-1284, but much shorter than the duration of the 5-HIAA rise and the 5-HT decrease. After Ro 4-1284, the duration of the enhancement of 5-HTP corresponded to the rise of 5-HIAA and the decrease of 5-HT. The results indicate that both Ro 4-1284 and reserpine increase the synthesis of 5-HT, possibly via a feedback mechanism originating from presynaptic and/or postsynaptic 5-HT receptors. It is also suggested that the increase of the 5-HIAA concentration after the drugs is probably due to the metabolism of the 5-HT originating from the 5-HT storage depots which are rapidly depleted by the drugs and of the 5-HT formed by enhanced synthesis. 19 references.

002264 Sato, Mitsumoto; Hikasa, Naotomo; Tomoda, Takako; Suemaru, Koso; Otsuki, Saburo. Dept. of Neuropsychiatry, School of Medicine, Okayama University Okayama, Japan **Seizure development and dopamine receptor sensitivity.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 32(3):343-344, 1978.

Seizure development and dopamine receptor sensitivity are described. The relationship between seizure development and receptor sensitivity of dopaminergic neuron systems in the amygdaloid kindling under the chronic cocaine pretreatment, haloperidol treatment, and in the drug free state. All cocaine pretreated animals showed not only the reverse tolerance phenomenon but also sensitization to apomorphine. The results suggest strongly that dopamine receptor sensitivity may be an important factor in the kindling seizure development and establishment of its underlying transsynaptic change in the brain. 9 references.

002265 Scatton, B.; Dedek, J.; Korf, J. Synthelabo, LERS, Department of Biology, Neurochemistry Unit, Bagneux, France **Dopamine metabolism in the rat retina and brain after acute and repeated treatment with neuroleptics.** Advances in Biochemical Psychopharmacology. 19:373-375, 1978.

The effects of chronic neuroleptic treatment on dopamine (DA) turnover in various regions of the male rat brain were examined. Repeated treatment with high doses of the classical neuroleptic haloperidol (5mg/kg i.p.)or the atypical neuroleptic sulpiride (100mg/kg i.p.)for 11 days induced tolerance to the increases in DA metabolites in all cerebral structures studied, but regional differences were observed. The threshold dose for inducing tolerance in the striatum was lower than that for other brain areas, and no tolerance was observed in retina. Moreover, repeated administration of a low dose (0.2mg/kg i.p.)of haloperidol-induced tolerance more rapidly in the striatum than in mesolimbic areas and did not induce tolerance in the frontal cortex. Cross-tolerance between the two neuroleptics was demonstrated, indicating the tolerance was probably not related to enzyme induction. It is suggested that tolerance to the neuroleptic-induced increase in DA turnover may be a biological correlate of supersensitivity of presynaptic or postsynaptic or DA Receptors. 11 references.

002266 Scherer-Singler, U.; McGeer, E. G. Kinsmen Laboratory of Neurological Research, Dept. of Psychiatry, University of British Columbia, Vancouver, BC, Canada V6T 1W5 **Distribution and persistence of kainic acid in brain.** Life Sciences (Oxford). 24(11):1015-1022, 1979.

The distribution of tritiated kainic acid in male Wistar rat brain was studied as a function of time after injection of 5nmoles into the neostriatum, substantia nigra, or cerebellum. More than half of the injected material disappeared from the injection site and the brain within one half hour of injection. Very small amounts of radioactivity (less than 7pmol/mg tissue) were found in areas other than the injection sites, suggesting that the histological damage reported in the hippocampus and pyriform cortex after striatal injections may be due to a secondary process not dependent on the presence of toxic concentrations of kainic acid in those areas. The bulk of the kainic acid did not appear to be metabolized rapidly. 8 references. (Author abstract modified)

002267 Schmidt, Richard H.; Bhatnagar, Ranbir K. Department of Pharmacology, University of Iowa, Iowa City, IA 52242 **Regional development of norepinephrine, dopamine-beta-hydroxylase and tyrosine hydroxylase in the rat brain subsequent to neonatal treatment with subcutaneous 6-hydroxydopamine.** Brain Research (Amsterdam). 166(2):293-308, 1979.

In neonatal Sprague-Dawley rats injected subcutaneously with 100mg/kg 6-hydroxydopamine (6-OHDA) on postnatal days 1, 2 and 3, extensive degeneration of noradrenergic nerve terminals in parietal cortex and cerebellum was evident by postnatal day 4, with norepinephrine (NE) levels and dopamine-beta-hydroxylase (DBH) activities reduced by more than 80% and tyrosine hydroxylase (TOH) activities reduced by 50%. In the parietal cortex, noradrenergic degeneration remained complete; at 9 and 70 days after birth NE concentration and DBH and TOH activities were all decreased by 90 to 95%. In the cerebellum, a progressive regeneration and apparent sprouting of NE fibers was observed; by postnatal day 9, NE, DBH, and TOH had recovered to near control levels, and by day 70 these measures exceeded control levels by 95, 115, and 50%, respectively. In the pons/medulla, the intial effect of 6-OHDA was neglible, but NE content increased by postnatal day 9 and surpassed control level by 70% on day 70. On day 70, NE level and DBH activity were increased more substantially in the rostal half of the pons, than in the pons/medulla as a whole. Results indicate that the initial amount of degeneration induced by 6-OHDA is similar in the parietal cortex and cerebellum, but regeneration proceeds only in the cerebellum. This suggests that noradrenergic fiber growth and regeneration in each target tissue is under independent regulation, possibly by the individual target neurons themselves. 46 references. (Author abstract modified)

002268 Schmidt, Richard H.; Bhatnagar, Ranbir K. Department of Pharmacology, University of Iowa, Iowa City, IA

52242 **Assessment of the effects of neonatal subcutaneous 6-hydroxydopamine on noradrenergic and dopaminergic innervation of the cerebral cortex.** Brain Research (Amsterdam). 166(2):309-319, 1979.

Unilateral electrolytic lesions of the locus coeruleus were made at 112 days of age in female Sprague-Dawley rats that had been treated subcutaneously with 6-hydroxydopamine (6-OHDA) or vehicle at birth. In the vehicle treated rats, the locus coeruleus lesion resulted in at least an 80% reduction of norepinephrine (NE) and dopamine-beta-hydroxylase (DBH) in the ipsilateral telencephalon, relative to the contralateral side. Tyrosine hyroxylase (TOH) was reduced to a similar extent only in the parietal cortex and hippocampus. In the prefrontal cortex and cingulate gyrus, TOH was decreased by only 31 and 64%, respectively; the remainder was apparently associated with projections of the mesocortical dopamine (DA) system. The ratio of TOH to DA in dopaminergic terminals was about 10 times greater than the ratio of TOH to NE in noradrenergic terminals. Neonatal 6-OHDA treatment resulted in near total elimination of noradrenergic terminals throughout the telencephalon, and the locus coeruleus lesion had no additional effect. The drug treatment produced no significant change in DA content or in the TOH to DA ratio in the prefrontal cortex and cingulate gyrus, indicating complete sparing of the mesocortical DA projections. 29 references. (Author abstract modified)

002269 Schulz, Rudiger; Faase, Elisabeth; Wuster, Michael; Herz, Albert. Dept. of Neuropharmacology, Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse 2, D-8000 Munich 40, Germany **Selective receptors for beta-endorphin on the rat vas deferens.** Life Sciences (Oxford). 24(9):843-849, 1979.

Electrically evoked twitches of the rat vas deferens were not depressed by morphine, but were inhibited by the opioid peptide beta-endorphin, with half maximal inhibition at 100nM. Fragments of beta-endorphin (methionine-enkephalin, alpha-endorphin, and gamma-endorphin) were almost ineffective. The opiate alkaloid etorphine, a powerful inhibitor of guinea-pig ileum and mouse vas deferens, was 100 times less potent on the rat vas deferens preparation. These results suggest that the rat vas deferens may contain a selective type of opioid receptor, unrelated to the mu and delta receptors so far described for opioids on isolated preparations. 21 references. (Author abstract modified)

002270 Schwendener, Reto A.; Weder, Hans-Georg. Pharmaceutical Institute, Dept. of Physical Pharmacy, Swiss Federal Institute of Technology, Zurich CH-8093, Switzerland **The binding of chlorpromazine to bilayer liposomes. Evaluation of stoichiometric constants from equilibrium and steady state studies.** Biochemical Pharmacology (Oxford). 27(23):2721-2727, 1978.

The influence of the amount of cholesterol incorporated into egg yolk bilayer liposomes on the binding of chlorpromazine was examined. The binding of chlorpromazine was evaluated in terms of stoichiometric constants and showed a strong positive cooperative binding step, followed by an equally strong negative cooperative step. The first step may be related to the partition of chlorpromazine into the lipophilic bilayer core, whereas the second and the following steps describe the overall saturation of the liposome membrane. It is concluded that the binding of chlorpromazine is attenuated by increasing amounts of cholesterol present in the bilayer liposomes. 20 references. (Author abstract modified)

002271 Scotti de Carolis, A.; Florio, V.; Longo, V. G. Laboratorio di Farmacologia, Istituto Superiore di Sanita, Rome, Italy **Further analysis of the effects of harmine on the electrical activity of the rabbit brain.** Neuropharmacology (Oxford). 17(4/5):295-298, 1978.

The effects of harmine on the electrical activity of the red nucleus, nucleus ventralis anterior of the thalamus, head of nucleus caudatus, and hypothalamus were studied in the rabbit. Harmine induced, at the level of the red nuclei, synchronous waves at 10 cycles/second. These patterns were not modified by pretreatment with diazepam (1mg/kg, iv). However, diazepam alone modified the electrical activity of the red nucleus, diminishing the frequency and increasing the voltage of the waves. The same patterns could be obtained after administration of barbiturates and meprobamate but not after diphenylhydantoin. 10 references. (Author abstract modified)

002272 Seeber, U.; Kuschinsky, K.; Sontag, K.-H. Institut fur Biochemische Pharmakologie, Max Planck Institut fur Experimentelle Medizin, Hermann-Rein-Strasse 3, D-3400 Gottingen, Germany **Inhibition by opiate narcotics of rat flexor alpha-motoneurones.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 301(3):181-185, 1978.

Specific effects of opiate narcotics on rat flexor alpha-motoneurons were studied in ventral roots of laminectomized rats under halothane anesthesia. The alpha-motoneurons were activated by tetanic stimulation of the cut ipsilateral common peroneal nerve, exciting up to Group II but not Group III and C-afferents. Morphine (0.5-3.0mg/kg, i.v.)reduced or completely suppressed the discharge rate of flexor alpha motoneurons in a dose dependent matter. This effect was antagonized by naloxone (0/5mg/kg, i.v.)and mimicked by levorphanol (1.0mg/kg, i.v.), but not by an equal dose of stereoisomer dextrophan, suggesting that the effect of morphine was abolished. The action of opiates leading to inhibition of flexor alpha-motoneurons may contribute to akinesia and catalepsy, and opioid-induced muscular rigidity. Findings suggest that morphine produces a reciprocal change in activity evoked in extensor and flexor reflex pathways. 10 references. (Author abstract modified)

002273 Sethy, Vimala H. CNS Disease Research, The Upjohn Company, Kalamazoo, MI 49001 **Effect of hypnotic and anxiolytic agents on regional concentration of acetylcholine in rat brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 301(3):157-161, 1978.

The effect of hypnotic and anxiolytic agents on regional concentration of acetylcholine in rat brain was studied. Pentobarbital (30 and 60mg/kg) and chloral hydrate (300 and 600mg/kg) administered in anesthetic/hypnotic doses produced significant increases in acetylcholine concentration in the cerebral cortex, striatum, hippocampus and brainstem. Hypnotic anxiolytic agents like diazepam, flurazepam (100mg/kg each) and triazolam (30mg/kg) significantly increased the acetylcholine concentration only in the cerebral cortex and striatum. Alprazolam and ketazolam had no significant effect on regional distribution of acetylcholine in the brain. The correlation between the depression of the central nervous system, as rated by sedation and loss of righting reflex, and an increase in acetylcholine concentrations in the discrete areas of the rat brain suggest that central cholinergic neurons may play a significant role in anesthesia and sleep. 23 references. (Author abstract modified)

002274 Severson, J. A.; Finch, C. E. no address **Dopamine receptors in the striatum of C57BL/6J male mice during aging.** Gerontological Society: 31st Annual Scientific Meeting. 18(5, Part 2):121, 1978.

A summary of a paper read at the 31st Annual Meeting of the Gerontological Society, held in Dallas, November 1978, is presented. Binding in the striatal membranes of C57BL/6J male mice during aging were assessed via use of an assay derived from the binding of 3H-spiroperidol to membranes prepared from human and rodent brain regions. Total binding capacity in

fM/mg protein was 123.2plus or minus 15.5at 3 months, 118.9plus or minus 11.0at 8 months, and 88.2plus or minus 14.8at 28 months. Scatchard analysis revealed no age related change in the dissociation constant. These age related changes paralleled reported decreases in dopamine sensitive adenyl cyclase in the rat corpus striatum. Results indicated that losses of dopamine responsive components within the corpus striatum underlie other functional impairments within this brain structure, including altered behavioral responses to butyrophenome neuroleptics. (Author abstract modified)

002275 Sharpe, L. G.; Garnett, Janie E.; Olsen, Nancy S. NIDA, Addiction Research Center, P. O. Box 12390, Lexington, KY 40583 **Thermoregulatory changes to cholinomimetics and angiotensin II, but not to the monoamines microinjected into the brain stem of the rabbit.** Neuropharmacology (Oxford). 18(2):117-125, 1979.

The effects of microinjection of the monoamines (dopamine, norepinephrine, epinephrine, and 5-hydroxytryptamine), carbachol, acetylcholine, eserine, and angiotensin II into several basal forebrain and brainstem sites on the thermoregulatory responses of male New Zealand white rabbits were investigated. The monoamines (0.75-100mcg) failed to evoke consistent changes in brain or colonic temperature when injected in several preoptic, diencephalic, mesencephalic, and lower brainstem sites. Carbachol (0.375-6mcg) produced a dose dependent rise in temperature when microinjected into the medial and lateral preoptic area, bed nucleus of the stria terminalis, anterior and posterior hypothalamic area, and mesencephalic and pontine central gray. Microinjections of cholinomimetics into the fourth ventricle evoked a consistent fall in temperature. Angiotensin II (0.05-1.5mcg) produced a dose dependent fall in body temperature when injected in the lateral basal forebrain and medial aspects of the hypothalamus, thalamus, midbrain, and pons. Results suggest that central monoamines play no role (or a very minor one) in the central control of thermoregulation in the rabbit; central cholinergic systems appear to function in heat gain and possibly heat loss mechanisms, and angiotensin II appears to be involved in the activation of heat loss mechanisms. 40 references. (Author abstract modified)

002276 Shenoy, Ananth K.; Ziance, Ronald J. Department of Pharmacology, School of Pharmacy, University of Georgia, Athens, GA 30602 **Comparative regulation of potassium and amphetamine-induced release of 3H-norepinephrine from rat brain via presynaptic mechanisms.** Life Sciences (Oxford). 24(3):255-264, 1979.

The ability of various drugs to modify the potassium (K) or d-amphetamine (d-A) induced release of tritiated norepinephrine (3H-NE) from chopped male Sprague-Dawley rat cortical tissue was examined. The K-induced release of 3H-NE was significantly reduced by the beta-receptor antagonist propranolol, the alpha-receptor agonist clonidine, and prostaglandin E2. Pretreatment with the prostaglandin synthesis inhibitor eicosatetrynoic acid did not influence the effect of clonidine on 3H-NE release. Exogenous l-NE, but not d-NE, decreased release of the transmitter. Blockade of alpha-receptors by phentolamine or stimulation of beta-receptors by isoproterenol significantly enhanced the K-induced release of 3H-NE from cortical tissue. The d-A-induced release of 3H-NE was reduced by propranolol and clonidine, but was not altered by phentolamine, isoproterenol, or prostaglandin E2. Results indicate that the K-induced release of 3H-NE from cortical tissue is modified by presynaptic negative and positive feedback mechanisms, that are mediated by alpha-receptors and beta-receptors, respectively, while the d-A-induced release of 3H-NE is not. 41 references. (Author abstract modified)

002277 Siemens, Albert J.; Doyle, Olivia L. Research Institute on Alcoholism, 1021 Main Street, Buffalo, NY 14203 **Cross-tolerance between delta9-tetrahydrocannabinol and ethanol: the role of drug disposition.** Pharmacology Biochemistry and Behavior. 10(1):49-55, 1979.

Acute challenge of delta9-tetrahydrocannabinol (THC, 10.1mg/kg), administered intragastrically by gavage (IG), or ethanol (1.24g/kg ip), reduced the rotarod performance of female CD rats by 50%. Daily treatment with THC (10.1mg/kg IG) or ethanol (4g/kg IG) resulted in tolerance to the effects of challenge doses of both drugs on rotarod performance. THC tolerant animals were cross-tolerant to the challenge dose of ethanol, but ethanol tolerant rats did not show complete cross-tolerance to the challenge dose of THC. THC tolerant animals initially had higher blood levels of 14C-THC than controls after IG drug administration; following intravenous injection, the rates of 14C-THC disappearances were equivalent. The disappearance of 14C-THC was not altered in ethanol tolerant rats, and the rates of ethanol disappearance were not significantly modified in ethanol or THC tolerant animals. 32 references. (Author abstract modified)

002278 Simpson, C. W.; Ruwe, W. D.; Malven, P. V.; Myers, R. D. Department of Psychological, Biological and Animal Sciences, Purdue University, West Lafayette, IN 47907 **Serum thyroxin levels during hyperthermia evoked in the monkey by intrahypothalamic injection of PGE1, 5-HT or pyrogen.** Brain Research Bulletin. 3(3):275-278, 1978.

Serotonin (5-HT), prostaglandin E1 (PGE1), or a bacterial pyrogen (E. coli or S. typhosa) was microinjected in a volume of 1.0-1.5mcl into the hypothalamus of an unanesthetized monkey to evoke a long-term hyperthermia and measure serum thyroxin levels. Samples of venous blood collected every 15 minutes before, during, and after each fever were analyzed by radioimmunoassay for plasma thyroxin levels. There was no statistically significant correlation between plasma thyroxin values and a given phase of the hyperthermic episode induced by the microinjections of 5-HT, PGE1, or bacteria. The possibility that an enhanced release of the thyroid hormone serves to sustain a long-term elevation in temperature evoked by a centrally acting pyrogenic substance is not supported. 17 references. (Author abstract)

002279 Skau, K. A.; Gerald, M. C. Division of Pharmacology, College of Pharmacy, Ohio State University, 500 West 12th Avenue, Columbus, OH 43210 **Curare-like effects of the amphetamine isomers on neuromuscular transmission.** Neuropharmacology (Oxford). 17(4/5):271-276, 1978.

The neuromuscular blocking effects of the amphetamine isomers were evaluated for possible actions via the adrenergic and cholinergic systems in the isolated Sprague-Dawley rat phrenic nerve diaphragm preparation. Dopaminergic, alpha-adrenergic, and beta-adrenergic receptor blockers failed to modify the blocking effects of amphetamine on nerve stimulated diaphragms, suggesting the absence of catecholaminergic innervation. In chronically denervated diaphragms, amphetamine and the nondepolarizing blocker ()-tubocurarine shifted the acetylcholine concentration response curve to the right and failed to produce muscle contracture; the latter effect was produced by the depolarizing blocker succinylcholine. Physostigmine and potassium chloride reversed amphetamine and tubocurarine blockade, but not that elicited by succinylcholine. Tetanus and posttetanic potentiation were depressed in a concentration dependent manner by amphetamine isomers, with the ()-isomer 1.8times more potent than its (-)-enantiomer. 24 references. (Author abstract modified)

002280 Slater, P.; Blundell, C. Dept. of Physiology, Medical School, University of Manchester, Manchester M13 9PT, England **The effects of a permanent and selective depletion of brain catecholamines on the antinociceptive action of morphine.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 305(3):227-232, 1978.

The effects of a permanent and selective depletion of brain catecholamines on the antinociceptive action of morphine was investigated via administration of 6-hydroxy dopamine to newborn mice. After 60 days, their brains were deficient in noradrenaline and dopamine while morphine's antinociceptive action was reduced. Adult rat and mice brains were treated with 6-hydroxydopa; brain noradrenaline was reduced in both species, but the antinociceptive action of morphine was reduced only in adult mice. It is concluded that in the mouse the antinociceptive action of morphine relies in part on normal brain noradrenaline function and dopamine is not directly involved. In the rat, morphine's action is affected by neurotoxic drugs which alter brain dopamine function. 33 references. (Author abstract modified)

002281 Snider, Stuart R. Health Sciences, Columbia University, New York, NY **Morphine: acute effects on adrenal dopamine release. (Unpublished paper).** Final Report, NIMH Grant R03-MH-30129, 1978. 7 p.

Stimulation of the sympathetic autonomic nervous system in rats was attempted with large dose morphine injections, and the adrenal, plasma, and brain levels of catecholamines before and after injection were measured. The turnover of specific catecholamines, dopamine (DA) and norepinephrine plus epinephrine (NE plus E), was also determined by measuring the formation of these substances from 3H-tyrosine precursor and by measuring their disappearance rates after synthesis inhibition with alpha-methltyrosine and NSD-1015. A morphine dosage of 30mg/kg effectively stimulated the sympathetic nervous system. Although results confirmed expectations, the mechanism of the observed increase in peripheral DA, in the absence of an increase in NE plus E, is unexplained.

002282 Souto, M.; Monti, J. M.; Altier, H. Departamento de Farmacologia y Terapeutica, Hospital de Clinicas, Montevideo, Uruguay **Effects of clozapine on the activity of central dopaminergic and noradrenergic neurons.** Pharmacology Biochemistry and Behavior. 10(1):5-9, 1979.

The effects of clozapine on the spontaneous firing of noradrenergic (NE) neurons in the locus coeruleus, dopaminergic (DA) neurons in the zonal compacta and ventral tegmental area, and nondopaminergic neurons in the zona reticulata were studied in male Wistar rats anesthetized with chloral hydrate. Clozapine significantly increased the spontaneous activity of NE and DA neurons. After a cumulative dose of 8mg/kg ip clozapine, the increase of mean firing rate per minute was similar in zona compacta and ventral tegmental area neurons. Zona reticulata neurons were depressed by clozapine, neither amphetamine nor physostigmine antagonized the inhibition. Results suggest that clozapine blocks central NE and DA receptors. No evidence for a smaller sensitivity of the striatum to clozapine, as compared to the limbic system, was obtained. 20 references. (Author abstract modified)

002283 Stein, J. M.; Wayner, M. J.; Kantak, K. M.; Adler-Stein, R. L. Brain Research Laboratory, Syracuse University, 601 University Avenue, Syracuse, NY 13210 **Synergistic action of p-chloroamphetamine and fluoxetine on food and water consumption patterns in the rat.** Pharmacology Biochemistry and Behavior. 9(5):677-685, 1978.

The distribution of eating, drinking, and body weight changes during the 24 hour day were examined following brain serotonin (5-HT) depletion with p-chloroamphetamine (PCA) in both rats pretreated with fluoxetine and nonpretreated animals. Following a baseline period, measurements of food and water intakes and body weights were recorded 1, 2, 3, 6, 12, 20, and 24 hours following PCA or saline administration. Results indicate acute hypophagia, hypodipsia, and body weight losses. These decreases were not influenced by the time of day when PCA was administered. Pretreatment with fluoxetine enhanced rather than blocked these effects. 41 references. (Author abstract modified)

002284 Steinsland, Odd S.; Hieble, J. Paul. Dept. of Pharmacology and Toxicology, University of Texas Medical Branch, Galveston, TX 77550 **Dopaminergic inhibition of adrenergic neurotransmission as a model for studies on dopamine receptor mechanisms.** Science. 199(4327):443-445, 1978.

Dopaminergic inhibition of adrenergic neurotransmission was investigated as a model for studies on dopamine receptor mechanisms. Dopamine and apomorphine produced concentration dependent inhibition of adrenergic neurotransmission in the isolated, perfused, rabbit ear artery. The inhibitory action of both dopamine and apomorphine was competitively antagonized by haloperidol and several other antipsychotic drugs. The calculated affinities of these drugs for the dopaminergic receptor correlate closely with both the pharmacological potencies of these drugs in vivo and their reported potencies as inhibitors of (3H) haloperidol binding to dopamine receptors in brain homogenates. 15 references. (Author abstract modified)

002285 Stewart, Jane; Eikelboom, Roelof. Dept. of Psychology, Concordia University, 1455 de Maisonneuve Blvd., Montreal, Quebec, Canada, H3G 1M8 **Pre-exposure to morphine and the attenuation of conditioned taste aversion in rats.** Pharmacology Biochemistry and Behavior. 9(5):639-645, 1978.

Three experiments using male Wistar rats to investigate the relationship between the mechanisms underlying the attenuation of a conditioned taste aversion to morphine by preexposure to the drug and the development of tolerance to the analgesic response to morphine are described. It was found that different environments for the preexposure injections and for the conditioning injections had no effect on the attenuation of the taste aversion. Attenuation of the analgesic effect was found to be specific to the environment in which repeated injections were given. It is concluded that different associative processes are responsible for the two types of attenuation. 30 references. (Author abstract modified)

002286 Stock, G.; Heidt, H.; Buss, J.; Schlor, K. H. Dept. of Physiology, University of Heidelberg, D-6900 Heidelberg, Germany **Sleep patterns in cat induced by gamma-hydroxybutyric acid.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 44(4):523-527, 1978.

The effect of intravenous injections of gamma-hydroxybutyric acid (GABA upon cat sleep pattern was measured. As shown by data from the EEG, eye movements, the neck electromyograph, heartrate, and arterial pressure, GABA injection (150 to 200 mg/kg) was able to induce slow wave sleep (SWS) as well as desynchronized sleep (DS). The decreases in arterial pressure were not different from those recorded during naturally occurring DS. GHBA, given at doses above 200 mg/kg induced anesthesia, during which arterial pressure was elevated. At the end of GHBA-induced sleep or anesthesia there was a stage during which the animals were ataxic. The EEG showed a hypersynchronous spike pattern and arterial pressure was markedly elevated. 12 references. (Author abstract modified)

002287 Stone, Trevor W. Department of Physiology, St. George's Hospital Medical School, University of London,

London SW17 ORE, England **Selective antagonism of amino acids by alpha-aminoadipate on pyramidal tract neurones but not Purkinje cells.** Brain Research (Amsterdam). 166(1):217-220, 1979.

The ability of alpha-aminoadipate (aAA) to antagonize responses to glutamate and aspartate on pyramidal tract cells in the cerebellar cortex and Purkinje cells in the cerebellum was studied in male rats anesthetized with urethane. In pyramidal tract neurons, aAA reduced by more than 50% the peak amplitude of responses to the amino acids, without affecting acetylcholine or hydrogen ion excitations. An ability of aAA to differentiate between glutamate and aspartate was seen in 9 of 21 pyramidal tract neurons. In Purkinje cells, aAA was able to reduce responses to the excitatory amino acids without affecting acetylcholine or hydrogen ion excitations, but no differential blockade of aspartate and glutamate was observed. The finding that aAA differentiates between aspartate and glutamate in pyramidal tract cells but not in Purkinje cells suggests that the amino acid receptors on the two cell types differ in their pharmacological properties or in their spatial distribution. 15 references.

002288 Stone, Trevor W.; Taylor, David A. Taylor: Dept. of Pharmacology, University of Colorado Medical Center, Denver, CO 80220 **Clonidine as an adenosine antagonist.** Journal of Pharmacy and Pharmacology (London). 30(12):792-793, 1978.

The effects of clonidine on neuronal responses to adenosine were studied in vivo in rats. When applied microiontophoretically to neurons in the motorsensory areas of the cerebral cortex, adenosine depressed all 26 neurons tested. At least one of the two control agonists used, noradrenaline and 5-hydroxytryptamine (5-HT), also depressed each cell tested. When clonidine was ejected with currents greater than 25nA, there was usually a marked depression of neuronal firing. However, the ejection of clonidine with currents of less than 25nA resulted in a block of neuronal responses to adenosine in 22 of the 26 cells tested, with no change in responses to control amines. Thus, clonidine blocks neuronal depressant responses to adenosine at doses that do not produce direct depression of cell firing or interfere with noradrenaline or 5-HT. 11 references.

002289 Sun, G. Y.; Creech, D. M.; Sun, A. Y.; Samorajski, T. Sinclair Comparative Medicine Research Farm, University of Missouri, Columbia, MO 65211 **Effects of ethanol and dihydroergotoxine on mouse brain myelin components.** Research Communications in Chemical Pathology and Pharmacology. 22(3):617-620, 1978.

The effects of prolonged consumption of ethanol, dihydroergotoxine (Hydergine) and Hydergine plus ethanol on brain myelin components isolated from the medulla oblongata of mouse brain were examined. Based on protein content, the amount of myelin isolated from the brain tissue was not different with regard to the various treatments. However, there was a significant decrease (20%) in myeline phospholipid and cholesterol to protein ratios in the ethanol group as compared to controls and the Hydergine treated group. Hydergine and Hydergine plus ethanol groups had higher cholesterol to phospholipid ratios than controls. 18 references. (Author abstract modified)

002290 Sunahara, G. I.; Kalant, H.; Schofield, M.; Grupp, L. Dept. of Pharmacology, University of Toronto, Toronto, Ontario, Canada M5S 1A8 **Regional distribution of ethanol in the rat brain.** Canadian Journal of Physiology and Pharmacology (Ottawa). 56(6):988-992, 1978.

Ethanol concentrations in cortex, striatum, and hippocampus were compared with arterial and venous blood alcohol concentrations following ip or iv injections in male Wistar rats. Equilibrium between tissue and arterial blood occurred within 3 minutes and followed simple diffusion kinetics. Equilibrium between tissue and venous blood required 10-15 minutes and coincided with the disappearance of the arterial/venous difference. Results suggest that tissue ethanol concentrations cannot be determined from venous blood samples until brain arteriovenous equilibrium has occurred and that alcohol concentrations in tissue perfusates do not necessarily provide a reliable guide to those in tissue. 31 references. (Author abstract modified)

002291 Svorad, D.; Lukovic, L. Institute of Normal and Pathological Physiology, Slovak Academy of Sciences, Sienkiewiczova 1,884 23 Bratislava, Czechoslovakia **Changes of neuronal activity of the caudate nucleus after pentobarbital and curare.** Activitas Nervosa Superior (Praha). 20(2):103-105, 1978.

In a paper presented at the 14th Interdisciplinary Conference on the Experimental and Clinical Study of Higher Nervous Functions held at Marianske Lazne, Czechoslovakia, in October 1977, a study comparing the neuronal activity of the caudate nucleus of the rat under pentobarbital and curare was reported. The unit activity was recorded by extracellular tungsten microelectrodes in curalized nonanesthetized rats and in rats administered pentobarbital. It is concluded that the change of functional organization of the caudate under curare and pentobarbital is characterized also by a change of interspike histogram patterns. 4 references.

002292 Szerb, John C. Department of Physiology and Biophysics, Dalhousie University, Halifax, Nova Scotia, Canada B3H 4H7 **Relationship between Ca2-dependent and independent release of (3H)GABA evoked by high K, veratridine or electrical stimulation from rat cortical slices.** Journal of Neurochemistry (Oxford). 32(5):1565-1573, 1979.

The relationship between calcium (Ca2) dependent and independent release of exogenously labeled gamma-aminobutyric acid (GABA) induced by elevated potassium (K), veratridine, or electrical stimulation in Sprague-Dawley rat cortical slices was investigated. Results suggest that in the presence of Ca2, veratridine, high K and electrical stimulation release (3H)GABA from the same Ca2 dependent store. However, the absence of Ca2 enhances the release of (3H)GABA induced by veratridine or electrical stimulation from a Ca2 independent store. It is concluded that GABA release by veratridine or electrical stimulation is less Ca2 dependent than release induced by K. 44 references. (Author abstract modified)

002293 Tang, Siu W.; Helmeste, Daiga M.; Stancer, Harvey C. Dept. of Neurochemistry, Clark Institute of Psychiatry, University of Toronto, 250 College Street, Toronto, Canada M5T 1R8 **The effect of acute and chronic desipramine and amitriptyline treatment on rat brain total 3-methoxy-4-hydroxyphenylglycol.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 305(3):207-211, 1978.

The effect of acute (single dose), short-term (4 days), and chronic treatment (21 days) with two tricyclic antidepressants, desipramine and amitripyline on brain 3-methoxy-4-hydroxyphenylglycol (MHPG) was examined in the rat. Amitriptyline had no effect on brain total MHPG irrespective of the duration of the treatment and did not interfere with the lowering effect of clonidine on brain total MHPG. Acute and short-term desipramine treatment decreased brain total MHPG in rats, while chronic desipramine treatment increased it. The differential effect of acute and chronic treatment of desipramine on the brain total MHPG was further demonstrated by the lack of interference with the lowering effect of clonidine on brain total MHPG by one single dose of desipramine; partial interference after 4 days and complete inferference after 21 days of desipramine treatment. 29 references. (Author abstract modified)

002294 Taylor, Dorothy; Ho, Beng T. Texas Research Institute of Mental Sciences, 1300 Moursund Avenue, Houston, TX 77030 **Comparison of inhibition of monoamine uptake by cocaine, methylphenidate and amphetamine.** Research Communications in Chemical Pathology and Pharmacology. 21(1):67-75, 1978.

The effects of cocaine, methylphenidate, and amphetamine on biogenic amines were investigated using rat brains. Amphetamine and methylphenidate both inhibited the uptake of 3H-norepinephrine and 3H-dopamine, although the activity of d-amphetamine was lower with respect to uptake of the two catecholamines in synaptosomes from thalamus/hypothalamus and striatum. Cocaine was a much stronger inhibitor of 3H-5-hydroxytryptamine uptake in septum/caudate syaptosomes than amphetamine or methylphenidate. Results suggest that a serotonergic system may be involved in the stimulant properties of cocaine. This may explain certain differences in pharmacological activities between cocaine and the other two stimulants, as described in the literature. 21 references. (Author abstract modified)

002295 Tewari, S.; Duerbeck, Norman B.; Noble, E. P. Dept. of Psychiatry and Human Behavior, University of California, Irvine, CA 92727 **The effects of long term ethanol ingestion on RNA metabolism by inner membranes of rat brain mitochondria.** Research Communications in Chemical Pathology and Pharmacology. 22(2):401-418, 1978.

The effects of long-term ethanol ingestion on RNA metabolism by inner mitochondrial membranes in rats in rats were investigated. Ethanol ingestion is reported to affect the degree of incorporation of labeled RNA precursor into the mitochondrial RNA fraction at early time points, but not when the pulse time was extended to 5 days. Such results indicate the possibility of a rapid turnover rate for the brain mitochondrial RNA, with the ethanol group having a faster rate of turnover when compared to the control group. 30 references. (Author abstract modified)

002296 Tran, Vinh Tan; Snyder, Solomon H. Department of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Amino acid neurotransmitter candidates in rat cerebellum: selective effects of kainic acid lesions.** Brain Research (Amsterdam). 167(2):345-353, 1979.

In a study of the role of glutamate and gamma-aminobutyric acid (GABA) in cerebellar neuronal populations, the effects of cerebellar injection of kainic acid on endogenous levels and high affinity synaptosomal uptake of amino acids were studied in male Sprague-Dawley rats. It had previously been shown that injection of kainic acid into the cerebellum selectively destroys Purkinje, stellate, basket, and Golgi II cells, without altering granule cells. In the present study, kainic acid lesions produced a 65-70% decrease in high affinity tritiated GABA uptake into synaptosomal fractions and a similar decrease in glutamic acid decarboxylase, with a 50% reduction in endogenous GABA. Synaptosomal accumulation of tritiated glutamate and aspartate was reduced 25-30%, but no decline in uptake of other amino acids was observed. No significant changes were found in endogenous levels of glutamate, threonine, proline, alanine, valine, methionine, and isoleucine, but levels of glycine and serine were elevated. These findings are consistent with the possibility that glutamate is the transmitter of granule cells and that GABA is the transmitter of the other cell types in the cerebellum. 17 references. (Author abstract modified)

002297 Tripathi, Shephali; Pandey, B. R.; Raman, K.; Barthwal, J. P.; Kishor, K.; Bhargava K. P. Dept. of Pharmacology and Therapeutics, King George's Medical College, Lucknow University, Lucknow, India **Monoamine oxidase inhibiory and anticonvulsant properties of some newer thiosemicarbazones.** Research Communications in Chemical Pathology and Pharmacology. 22(2):291-300, 1978.

Eight 4-aryl-1-(2,3,4-trihydroxy acetophenone)-3-thiosemicarbazones were synthesized and evaluated for their anticonvulsant properties and for their ability to inhibit rat brain monoamine oxidase (MAO). All compounds exhibited concentration dependent inhibition of MAO. Anticonvulsant activity exhibited by these thiosemicarbazones against pentylenetetrazol-induced seizures ranged between 10% and 60%. 9 references. (Author abstract modified)

002298 Uchida, Shuji; Takeyasu, Kunio; Ichida, Seiji; Yoshida, Hiroshi. Department of Pharmacology I, Osaka University School of Medicine, Kita-ku, Osaka 530, Japan **Muscarinic cholinergic receptors in mammalian brain: differences between bindings of acetylcholine and atropine.** Japanese Journal of Pharmacology (Kyoto). 28(6):853-862, 1978.

Synaptic plasma membranes from Sprague-Dawley rat brain displayed reversible, high affinity binding sites for tritiated acetylcholine (ACh) and atropine. The dissociation constant values were 20nM for ACh and 1nM for atropine; maximal binding capacities were 0.8-1.2pmoles (1mg protein) for ACh and 1.5pmoles/mg protein for atropine. The specific binding of ACh was almost completely inhibited by oxotremorine and atropine. ACh binding was increased to about 1.5pmoles/mg protein by 5,5'-dithiobis(2-nitrobenzoic acid) (DTNB). DTNB also increased the ACh inhibition of atropine binding by about tenfold. Marked discrepancies in the inhibitions of atropine and ACh binding by muscarnic agonists, but not antagonists, were found. Results suggest that muscarinic receptors have different sites for agonists and antagonists. 23 references. (Author abstract modified)

002299 Uhl, George R.; Goodman, Robert R.; Kuhar, Michael J.; Childers, Steven R.; Snyder, Solomon H. Department of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Immunohistochemical mapping of enkephalin containing cell bodies, fibers and nerve terminals in the brain stem of the rat.** Brain Research (Amsterdam). 166(1):75-94, 1979.

Specific antisera to methionine-enkephalin and leucine-enkephalin were used to localize enkephalin containing cell bodies, fibers, and terminals in the brainstem of Sprague-Dawley rats. Cell bodies were found in the substantia gelatinosa and interpolaris zones of the trigeminal nuclear complex; the nucleus of the solitary tract; the vicinity of the nucleus raphe magnus; the dorsal cochlear, medial vestibular, and paraolivary nuclei; the parabrachial nuclei and dorsal tegmental nucleus of Gudden; the periaqueductal gray matter and interpeduncular nucleus; and along the borders of the lateral lemniscus and medial geniculate. In some areas, such as the parabrachial region, nucleus of the solitary tract, and substantia gelatinosa, these perikarya were associated with high densities of fibers and terminals. Other regions, such as the dorsal cochlear nucleus and the nucleus raphe magnus area, contained cell bodies associated with low densities of processes and terminals. In the nucleus of the facial nerve and the locus coeruleus, high fiber and terminal densities without associated cell bodies were evident. Many of these enkephalin localizations can be rationalized on the basis of known actions of opiate drugs and the brainstem distribution of opiate receptors. 35 references. (Author abstract modified)

002300 Ulus, I. H.; Wurtman, R. J.; Scally, M. C.; Hirsch, M. J. Dept. of Endocrinology, Massachusetts Institute of Technology, Cambridge, MA 02139 **Effect of choline on cholinergic function.** In: Jenden, D., Cholinergic mechanisms and psycho-

pharmacology. New York, Plenum, 1978. 885 p. Vol. 24. (p. 525-538).

At the third Symposium on Cholinergic Mechanisms and Psychopharmacology, held in La Jolla, CA, March 1977, a paper discussing the effect of choline (Ch) and acetylcholine (ACh) synthesis and the effects of Ch on cholinergic transmission was presented. Considerable evidence suggests that the concentration of free Ch in circulation is an important factor controlling the rate at which neurons make ACh. Experiments in which animals received Ch chloride indicate a dose dependent increase in serum Ch, brain Ch, and brain ACh levels. This indicates that the mechanisms by which Ch ingestion affects tissue ACh levels involves accelerated synthesis of the neurotransmitter and not simply decreased degradation. That Ch induced increases in neuronal ACh levels can affect the release of the transmitter was first shown indirectly by studies on the enzyme tyrosine hydroxylase in the dopaminergic terminal within the caudate nucleus. Increases in tyrosine hydroxylase activity after Ch administration have been observed in sympathetic ganglia and the adrenal medullae. Other investigations which show that treatments which cause prolonged elevations in the release of ACh, and produce parallel increases in tyrosine hydroxylase activity within the adrenal medullae and the sympathetic ganglia, are summarized. Those treatments include resperine administration, combination treatments of resperine and Ch, rats kept in the cold, and clinical studies which report that Ch administration ameliorates the signs of tardive dyskinesia. 36 references.

002301 Van Loon, Glen R.; De Souza, Errol B.; Kim, Chul. Dept. of Medicine, University of Toronto, Toronto, Ontario, Canada M5S 1A8 **Alterations in brain dopamine and serotonin metabolism during the development of tolerance to human beta-endorphin in rats.** Canadian Journal of Physiology and Pharmacology (Ottawa). 56(6):1067-1071, 1978.

The neurochemical and behavioral effects of acute and chronic intracisternal administration of human beta-endorphin to male Sprague-Dawley rats were examined. Acute administration of beta-endorphin produced catalepsy, analgesia, and hypothermia, but these effects were markedly decreased after the fourth injection. Acute administration of beta-endorphin increased neostriatal concentrations of 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA); the development of tolerance to beta-endorphin was associated with a decreased response of DOPAC and no change in the HVA response to beta-endorphin. The development of tolerance to repeated injections of beta-endorphin was also associated with increased 5-hydroxyindoleacetic acid concentrations in brainstem, hypothalamus, and hippocampus, compared to those in rats treated acutely with beta-endorphin or chronically with saline. Neither acute nor chronic treatment with beta-endorphin altered 5-hydroxtryptamine (5-HT) concentrations in the brain regions examined. Results suggest that the development of tolerance to the behavioral effects of beta-endorphin may be mediated by the development of tolerance to the effects of beta-endorphin on brain 5-HT and dopamine release. 31 references. (Author abstract modified)

002302 Vijayan, E.; McCann, S. M. Department of Physiology, University of Texas Health Science Center, 5323 Harry Hines Blvd., Dallas, TX 75235 **Blockade of dopamine (DA) receptors with pimozide and pituitary hormone release in response to intraventricular injection of gamma-aminobutyric acid (GABA) in conscious ovariectomized rats.** Brain Research (Amsterdam). 162(1):69-76, 1979.

The effect of intraventricular administration of gamma-aminobutyric acid (GABA) was evaluated in ovariectomized, female Sprague-Dawley rats pretreated with the dopamine (DA) receptor blocker pimozide (0.63mg/kg, subcutaneously). Pimozide alone markedly elevated prolactin levels, but had no other effect on plasma hormone levels. Intraventricular injections of 4mcM GABA elevated luteinizing hormone (LH) and growth hormone (GH) levels in both pimozide treated and control animals. The suppression of plasma thyrotropin (TSH) induced by GABA in intact animals was completely blocked in pimozide-treated rats. GABA reversed the pimozide-induced elevation of prolactin. It is concluded that dopaminergic systems are probably not involved in mediation of GABA effects on GH and LH, but that the GABA-induced inhibition of TSH may be mediated by stimulation of dopaminergic neurons which then inhibit release of thyrotropin releasing hormone. 22 references. (Author abstract modified)

002303 Vincent, Steven R.; McGeer, Edith G. Division of Neurological Sciences, Department of Psychiatry, University of British Columbia, Vancouver, British Columbia, Canada V6T 1W5 **Kainic acid binding to membranes of striatal neurons.** Life Sciences (Oxford). 24(3):265-270, 1979.

The specific binding of tritiated kainic acid to membrane fragments of male Wistar rat striatum was examined. The specific binding was saturable and of high affinity, with a dissociation constant of 71nM and maximal binding capacity of 254fM/mg protein. Lesions of the striatum by stereotaxic injection of 5nM kainic acid reduced the density of (3H)kainic acid binding sites by half, without affecting their affinity. Lesions of the corticostriatal afferents reduced sodium dependent glutamate uptake by 30%, but had no affect on binding of (3H)kainic acid. It is concluded that (3H)kainic acid binds to a population of receptors localized on neurons of the caudate putamen. 16 references. (Author abstract modified)

002304 Vocci, Frank J., Jr.; Karbowski, Michael J.; Dewey, William L. Department of Pharmacology, Box 726, Medical College of Virginia, Richmond, VA 23298 **Apparent in vivo acetylcholine turnover rate in whole mouse brain: evidence for a two compartment model by two independent kinetic analyses.** Journal of Neurochemistry (Oxford). 32(5):1417-1422, 1979.

Acetylcholine (ACh) turnover was determined in whole brains of male Swiss Webster ICR mice killed by microwave irradiation at various times (0.25-10 minutes) after pulse administration of (3H)choline (3H)-Ch. A precursor/product relationship was verified for Ch and ACh specific activities. Kinetic analyses by the biosynthesis ratio method and by finite differences method revealed two distinct turnover rats for ACh. In the first phase (0.25-1.5minutes after 3H-Ch injection), the ACh turnover rate averaged 22nmol/g/minute (both methods). During the second phase (2-10 minutes), the ACh turnover rates were significantly lower (7nmol/g/minute by the biosynthesis ratio method and 5.9nmol/g/minute by the finite differences method). Results are consistent with a two compartment model for ACh turnover in whole mouse brain. 19 references. (Author abstract modified)

002305 Waldmeier, Peter C.; Feldtrauer, Jean-Jacques; Kam, Roger; Stocklin, Kurt. Research Department, Pharmaceuticals Division, Ciba-Geigy AG, Basle, Switzerland **Effects of baclofen on striatal 5-HT mediated by the nigrostriatal dopamine system.** European Journal of Pharmacology (Amsterdam). 54(3):279-287, 1979.

Unilateral injection of baclofen into the substantia nigra increased dopamine (DA) and serotonin (5-HT) levels in the ipsilateral striata in female Tif: RAlf (SPF) rats. Homovanillic acid levels first declined and then increased to a maximum after 4 hours; 3,4-dihydroxyphenylacetic acid levels also increased after a latency of about 1 hour. These effects of baclofen on striatal DA metabolism suggest that the drug diminished impulse flow

in these DA neurons. DA metabolites were also found in greater quantities in the contralateral striata, probably reflecting compensatory activation of these DA neurons. Baclofen injected intranigrally did not increase the striatal 5-HT content in rats with 6-hydroxydopamine lesions of the nigrostriatal DA pathway. Results suggest that DA receptors are present on striatal 5-HT terminals or on interneurons that synapse axo/axonally with them. 23 references. (Author abstract modified)

002306 Walker, Peter; Weichsel, Morton E., Jr.; Fisher, David A.; Guo, Shirley M.; Fisher, Delbert A. Fetal-Maternal Research Laboratories, Los Angeles County Harbor-University of California-Los Angeles Medical Center, Torrance, CA 90509 **Thyroxine increases nerve growth factor concentration in adult mouse brain.** Science. 204(4391):427-429, 1979.

The effects of thyroxine and propylthiouracil on nerve growth factor concentrations in cerebral cortex, cerebellum, and brainstem of adult male mice were assessed using a sensitive radioimmunoassay for the beta-subunit of mouse nerve growth factor. Thyroxine administration significantly increased the concentration of nerve growth factor in all three brain areas compared to control values, whereas propylthiouracil was without effect. These results suggest that thyroid hormones stimulate nerve growth factor synthesis in the mature central nervous system, and raise the possibility that the influence of thyroid hormones on central nervous system development might be mediated or influenced by nerve growth factor. 22 references. (Author abstract)

002307 Waszczak, Barbara Lee. University of Michigan **The effects of chronic amphetamine administration upon mouse brain catecholamine content and synthesis. (Ph.D. dissertation).** Dissertation Abstracts International. 39(5):2249-B, 1978. Ann Arbor, Univ. Microfilms No. 7813753, 125p., 1978.

To determine the effects of repeated d-amphetamine administration upon regional catecholamine content and synthesis in the mouse brain, female, albino, and Swiss Webster mice were given d-amphetamine sulfate, 10 mg/kg, i.p.,every 6 hours for up to 10 days. At 2 day intervals during the period of drug administration, norepinephrine and dopamine content, tyrosine hydroxylase activity, and dopamine-beta-hydroxylase activity were determined in the following brain regions: brainstem, hypothalamus, anterior corpus striatum, and parietal cortex. Enzyme activities were determined in homogenates and tissue slices from various brain regions. Homogenate activity assays provided an index of the amounts of enzyme present. Kinetic studies with homogenates supplied information about amounts of enzyme as well as their activity for substrate or cofactor. Results show that repeated amphetamine administration caused an initial reduction in norepinephrine and dopamine content in all brain regions. In the brainstem, hypothalamus, and cortex, the levels of one or both amines approached control levels after 8 to 10 days of drug administration. Caudate catecholamine content is further reduced to about 50% of control values by 10 days of drug treatment. Regional changes in catecholamine content were correlated with changes in the activity and amount of tyrosine hydroxylase, suggesting that chronic amphetamine administration induces an increase in amount of tyrosine hydroxylase in certain brain regions. (Journal abstract modified)

002308 Weinberger, Susan B.; Knapp, Suzanne; Mandell, Arnold J. Department of Psychiatry, University of California at San Diego, La Jolla, CA 92093 **Failure of tryptophan load-induced increases in brain serotonin to alter food intake in the rat.** Life Sciences. 22(18):1595-1602, 1978.

The effects on food consumption of tryptophan injections, versus control saline treatment, were compared in 24 hour, food deprived rats at two time points in the rats' daily light/dark cycle. No effect of the two tryptophan doses, relative to the saline treatment, on food intake was observed, although tryptophan loading significantly raised brain tryptophan, serotonin, and 5-hydroxyindoleacetic acid levels in a dose dependent manner over baseline concentrations. Implications of these data for serotonergic modulation of food intake regulation are considered. 33 references. (Author abstract modified)

002309 Weiner, Cynthia D.; Collins, Michael A. Dept. of Biochemistry and Biophysics, Loyola University Stritch School of Medicine, Maywood, IL 60153 **Tetrahydroisoquinolines derived from catecholamines or DOPA: effects on brain tyrosine hydroxylase activity.** Biochemical Pharmacology (Oxford). 27(23):2699-2703, 1978.

Four different catecholic tetrahydroisoquinolines, cyclic condensation derivatives of L-DOPA, dopamine or noradrenaline and selected aldehydes, were examined for inhibition of rat brain tyrosine hydroxylase activity. Salsolinol, a condensate of dopamine and acetaldehyde which is implicated in the biological effects of alcohol, inhibited tyrosine hydroxylase in vitro; inhibition was competitive with pteridine cofactor. Tetrahydropapaveroline, a 1-benzyl derivative of dopamine also theorized to be involved in alcoholism, was markedly and significantly less effective than the other condensation products, since it inhibited tyrosine hydroxylase at relatively high concentrations only. It is concluded that inhibition of catecholamine biosynthesis remains a viable possibility if catechol tetrahydroisoquinolines are administered centrally or formed in neurons from condensations of catecholamines and aldehydes. 28 references. (Author abstract modified)

002310 Weisz, Donald Jacob. Kent State University **Effects of delta9-THC on CA1 pyramidal cell activity in rat hippocampus. (Ph.D. dissertation.)** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 7800363, HC$15. MF$7.50. 99 p. 1977.

In three experiments, the effects of delta9-tetrahydrocannabinol (THC) on two major responses of the CA1 pyramidal cell area to repetitive stimulation were examined in the rat hippocampus. The two responses investigated were low frequency potentiation and its relation to recurrent inhibition and self-sustaining afterdischarges of seizure activity. Over a wide range of doses the drug was found to increase spike latencies and increase recurrent inhibition. Moderate doses of THC excited CA1 pyramidal cell activity and lowered seizure thresholds. High doses depressed neuronal activity and increased seizure thresholds. (Journal abstract modified)

002311 Wheler, G. H. T.; Weller, J. L.; Klein, D. C. Laboratory of Developmental Neurobiology, Section on Neuroendocrinology, NICHHD, NIH, Bethesda, MD 20014 **Taurine: stimulation of pineal N-acetyltransferase activity and melatonin production via a beta-adrenergic mechanism.** Brain Research (Amsterdam). 166(1):65-74, 1979.

By stimulating the activity of N-acetyltransferase, taurine increased the conversion of tritiated tryptophan to tritiated N-acetylserotonin and melatonin by factors of 40 and 25, respectively, in male Sprague-Dawley rat pineal glands in organ culture. This stimulation was blocked stereospecifically by L-propranolol, indicating that taurine was probably acting via beta-adrenergic receptors. Taurine also stimulated N-acetyltransferase activity in denervated glands, indicating that it acts directly on the beta-adrenergic receptor. 14 references. (Author abstract modified)

002312 Wilkening, Doug; Makman, Maynard H. Laboratory of Biochemical Genetics, NHLBI, Bldg. 36, Rm. 1C06, NIH, Bethesda, MD 20014 **Effects of L-isopropylnorepinephrine, 3-isobu-**

tyl-1-methyl xanthine and dibutyryl cyclic AMP on hexose uptake and metabolism by rat striatal slices. Journal of Neurochemistry (Oxford). 32(5):1467-1472, 1979.

When rat striatal slices were incubated with either dibutyryl cyclic adenosine monophosphate (AMP) or with the beta-adrenergic agonist L-isopropylnorepinephrine (IPNE) plus the phosphodiesterase inhibitor 3-isobutyl-1-methylxanthine (IBMX), under conditions in which these agents stimulate glycogenolysis, significant alterations in hexose uptake were observed, as reflected in tritiated 2-deoxglucose (2-DOG) uptake, lactic acid formation, and oxygen consumption. The uptake of 3H-2-DOG was reduced by 20%-25% compared to basal uptake rates. The rate of lactic acid production was approximately doubled, and a small decrease in oxygen uptake was observed. These data are consistent with the conversion of the metabolism of a population of glycogen containing cells in the slices from primarily oxidative metabolism using an extracellular glucose source to primarily glycolytic metabolism using the cells' own glycogen stores, following incubation with dibutyryl cyclic AMP or IBMXIPNE. 21 references. (Author abstract modified)

002313 Wilkison, Douglas M.; Halpern, Lawrence M. Dept. of Pharmacology, School of Medicine, University of California, Davis, CA 95616 **Turnover kinetics of dopamine and norepinephrine in the forebrain after kindling in rats.** Neuropharmacology (Oxford). 18(2):219-222, 1979.

Turnover rate constants for dopamine (DA) and norepinephrine (NE) were estimated for the forebrain of kindled male Sprague-Dawley rats from which overt motor seizures had been elicited by stimulation of the basolateral amygdala. Kindled rats had significantly higher rate constants for DA turnover in the hemisphere ipsilateral to electrical stimulation. The turnover rate constant for DA in the contralateral hemisphere tended to be greater in kindled rats than in controls and was not significantly different from that in the ipsilateral hemisphere. NE turnover rate constants were not significantly different between groups of kindled and control rats. 9 references. (Author abstract modified)

002314 Williams, Michael; Risley, Edwin A. Neuropsychopharmacology Section, Merck Institute for Therapeutic Research, West Point, PA 19486 **Enhancement of the binding of 3H-diazepam to rat brain membranes in vitro by SQ 20009, a novel anxiolytic, gamma-aminobutyric acid (GABA) and muscimol.** Life Sciences (Oxford). 24(9):833-841, 1979.

Two anxiolytic compounds of the pyrazolepyridine carboxylic acid series, SQ 20009 and SQ 65396, enhanced the binding of tritiated diazepam to rat brain membranes in a concentration dependent manner. However. higher concentrations of these compounds (100mcM for SQ 20009 and 10mcM for SQ 65396) inhibited binding. Gamma-aminobutyric acid (GABA) and the GABA agonist muscimol also enhanced 3H-diazepam binding, whereas the GABA antagonist ()-bicuculline decreased binding. The effects of SQ 20009, the GABA agonists, and ()-bicuculline reflected changes in affinity rather than in number of binding sites. The effects of SQ 20009 and GABA are discussed in terms of an interaction with an endogenous diazepam-like factor. 31 references. (Author abstract modified)

002315 Wing, David R.; Paton, William D. M. Department of Pharmacology, University of Oxford, Oxford, England **Effects of acute delta1-tetrahydrocannabinol treatment, of hypothermia and of ambient temperature on choline incorporation into mouse brain.** Biochemical Pharmacology (Oxford). 28(2):253-260, 1979.

The effects of delta1-tetrahydrocannabinol (THC) and phenobarbitone on the incorporation of radioactivity into the brain after intravenous injection of (Me-14C)choline were studied in male CD-1 mice. The endogenous plasma choline level of 4.96mcg/ml was not affected by ip injection of THC. At an ambient temperature of 22 degrees, only the higher dose of THC (15mg/kg) influenced the appearance of label in the brain; incorporation into the lipid fraction fell by 52% and into the brain as a whole by 23%. Phenobarbitone (300mg/kg) had similar effects. Both drugs caused a marked lowering of rectal temperature in mice housed at 22 degrees, but this hypothermic effect was abolished at an ambient temperature of 33.5degrees. At this temperature, THC (15mg/kg) inhibited radioactive incorporation into the brain lipid fraction by 19%; phenobarbitone had a smaller effect, but also inhibited incorporation into the whole brain in the aqueous (19%) and lipid (23%) fractions. At 33.5degrees, the lower dose of THC (3.75mg/kg) caused an increase in incorporation into the brain aqueous (26%) and lipid (25%) fractions. 26 references. (Author abstract modified)

002316 Wirz-Justice, Anna; Krauchi, Kurt; Lichtsteiner, Maya; Feer, Hans. Psychiatrische Universitatsklinik, CH-4025 Basel, Switzerland **Is it possible to modify serotonin receptor sensitivity?** Life Sciences (Oxford). 23(12):1249-1254, 1978.

The possiblity of inducing serotonin receptor sensitivity after acute and chronic treatment with serotoninergic drugs was investigated in male albino Wistar rats. Results indicated that drugs acting on serotoninergic systems did not modify serotonin receptor sensitivity as measured by serotonin binding. Chronic 1-5HTP, the precursor amino acid, increased serotonin turnover but did not decrease serotonin binding. Chronic clomipramine, a predominantly serotonin uptake inhibitor, also had no effect on serotonin binding. In addition, chronic metergoline, a selective serotonin antagonist in the cortex, did not induce supersensitivity. This apparent intractability, of the serotonin receptor to changes after long-term treatment indicated a different postsynaptic regulatory mechanism than that found in catecholaminergic neurons. Futhermore, modification of serotonin receptor sensitivity is probably not relevant to the mode of action of antidepressant drugs. 17 references. (Author abstract modified)

002317 Wong, Chak-Lam; Bentley, Geoffrey A. Dept. of Pharmacology, Monash University, Clayton, Victoria, 3168 Australia **The effect of morphine pretreatment on hypothermia induced by morphine in mice.** European Journal of Pharmacology (Amsterdam). 53(4):391-394, 1979.

Subcutaneous administration of morphine to male Swiss mice produced a dose dependent hypothermia, which was antagonized by coadministration of naloxone. Pretreatment with a single dose of morphine induced tolerance to the hypothermic effect of a second dose of morphine given 3 hours later. Naloxone was more effective in antagonizing the hypothermic effect of morphine in morphine pretreated mice than in saline pretreated mice. Results indicate that morphine pretreatment can augment the antagonistic effect of naloxone toward the hypothermic action of morphine. 10 references. (Author abstract modified)

002318 Wood, J. D.; Mayer, C. J. Dept. of Physiology, University of Kansas Medical Center, Kansas City, KS 66103 **Slow synaptic excitation mediated by serotonin in Auerbach's plexus.** Nature (London). 276(5690):836-837, 1978.

In an investigation of the identity of the neurotransmitter of the slow excitatory postsynaptic potential (EPSP), it was found that application of serotonin (5-HT) to guinea-pig myenteric neurons mimics the slow EPSP. Results indicate that most of the criteria for establishing 5-HT as a neurotransmitter in Auerbach's plexus have been fulfilled: serotonin is synthesized and released by myenteric neurons; microiontophoresis of 5-HT mimics the action of the natural transmitter; actions of both the

natural transmitter and 5-HT are blocked by the 5-HT antagonist methysergide; tachyphylaxis occurs in exces 5-HT; inactivation mechanisms in the form of specific uptake of 5-HT exist in the myenteric plexus. It is suggested that a functional relationship between substance P and 5-HT exists. 16 references.

002319 Wood, Jeannette M.; Laverty, R. Department of Pharmacology, University of Otago Medical School, Dunedin, New Zealand **Physical dependence following prolonged ethanol or t-butanol administration to rats.** Pharmacology Biochemistry and Behavior. 10(1):113-119, 1979.

The physical dependence produced by prolonged administration of ethanol was compared with that produced by prolonged t-butanol administration in male Wistar rats, and the possible involvement of brain catecholamines in the development of alcohol dependence was examined. Withdrawal reactions were observed upon removal of either alcohol from the diet after 4 to 20 days, treatment. The range of withdrawal signs produced by the two alcohols was identical, but the time course of the withdrawal reactions differed. Administration of one alcohol prevented the appearance of a withdrawal reaction in rats dependent on the other alcohol. Depletion of brain noradrenaline and dopamine with 6-hydroxydopamine did not prevent the development of physical dependence on either alcohol. Thus, neither aldehyde formation nor brain catecholamines appear to be involved in the development of physical dependence on these alcohols. 29 references. (Author abstract modified)

002320 Wright, John W.; Donlon, Kate. Department of Psychology, Washington State University, Pullman, WA 99164 **Reversal of ethanol-induced body dehydration with prolonged consumption in rats.** Pharmacology Biochemistry and Behavior. 10(1):31-36, 1979.

Hypovolemia and carcass dehydration were observed in male Long-Evans hooded rats during the initial few days of forced choice maintenance on 10% ethanol. However, intravascular volume and carcass water returned to near normal levels after 2 months of forced consumption. Administration of exogenous antidiuretic hormone reduced to hypovolemia induced by ethanol, but carcass water level remained significantly diminished. 21 references. (Author abstract modified)

002321 Wu, Jang-Yen; Moss, Larry G.; Chude, Obi. Dept. of Cell Biology, Baylor College of Medicine, Texas Medical Center, Houston, TX 77030 **Distribution and tissue specificity of 4-aminobutyrate-2-oxoglutarate aminotransferase.** Neurochemical Research. 3(2):207-219, 1978.

A rapid and specific method for assaying 4-aminobutyrate-2-oxoglutarate aminotransferase (gamma-aminobutyric acid transaminase, GABA-T) was developed, based on the selectivity of ion exchange resin and the speed of vacuum filtration. Application of this method to mouse tissues yielded the following results: brain, 10.2; spinal cord, 11.8; liver, 5.7; kidney, 4.6; heart, 0.5; and lung, 0.4nmol glutamate formed/minute/mg. No activity was detected in muscle preparations. When the aminotransferases were tested with the antibody against the purified GABA-T from brain, no difference could be detected among brain, spinal cord, and kidney preparations. It is concluded that GABA-Ts from various tissues of the mouse are identical or closely related. 31 references. (Author abstract modified)

002322 Wuster, Michael; Herz, Albert. Abteilung fur Neuropharmakologie, Max Planck Institut fur Psychiatrie, Kraepelinstrasse 2, D-8000 Munchen 40, Germany **Opiate agonist action of antidiarrheal agents in vitro and in vivo -- findings in support for selective action.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 301(3):187-194, 1978.

Opiate agonist action of antidiarrheal agents was investigated in vivo and in vitro. In the radioreceptorassay, antidiarrheal agents completely inhibited the stereospecific binding of opiates in brain homogenates of rats, with affinities comparable to those of strong narcotic analgesics. Binding was increased in the absence of sodium. No differences in the affinities of these compounds to central and peripheral opiate receptors, respectively, were found. Antidiarrheal agents inhibited the electrically-induced contractions of the isolated longitudinal muscle myenteric plexus preparation of the guinea pig ileum. This effect was completely antagonized by naloxone. Compared to morphine, 3H-loperamide (injected i.v. in mice) was rapidly eliminated from the general circulation and only small concentrations reached the CNS. Up to 2 h after i.v. administration 3H-loperamide, an increase in radioactivity in the wall of small intestine was found. It may be concluded from the results that antidiarrheal compounds display agonist activity on opiate receptor sites in vivo and in vitro. 28 references. (Author abstract modified)

002323 Yaksh, Tony L.; Henry, James L. Dept. of Neurological Surgery, Mayo Foundation, Rochester, MN 55901 **Antinociceptive effects of intrathecally administered human beta-endorphin in the rat and cat.** Canadian Journal of Physiology and Pharmacology (Ottawa). 56(5):754-759, 1978.

The antinociceptive effects of intrathecally administered human beta-endorphin were investigated in rats and cats. Rats chronically implanted with intrathecal catheters displayed a dose dependent increase in the hot plate and tail flick response latencies following injection of human beta-endorphin into the lumbar spinal subarachnoid space through the indwelling catheter. Beta-endorphin was approximately 25 times more potent than morphine on a molar basis. Matching morphine and beta-endorphin doses such that approximately equal submaximal effects occurred, it was observed that the antinociception produced by beta-endorphin lasted approximately three times longer that that produced by morphine. Experiments with intrathecal injection of beta-endorphin into the spinal subarachnoid space of cats fitted with intrathecal catheters also revealed a potent antinociceptive effect which was completely antagonized by naloxone. In the rats, naloxone administered systemically in doses of 10-100mcg/kg produced a parallel shift in the dose/response curves of both nociceptive measures suggesting a competitive antagonism. These data and those derived from previous work based on the pA2 suggest that the interaction of morphine, certain pentapeptides, and beta-endorphin is the same with regard to the spinal opiate receptor population mediating behaviorally defined analgesia. 29 references. (Author abstract modified)

002324 Yamamoto, Iwao; Miki, Naomasa; Kondo, Shigeru; Kakiuchi, Shiro. Department of Pharmacology, Osaka University, Osaka 530, Japan **Effect of sodium ion on levels of cyclic adenosine 3',5'-monophosphate in guinea pig cerebral slices.** Japanese Journal of Pharmacology (Kyoto). 28(3):375-381, 1978.

Accumulation of cyclic AMP was studied in guinea pig cerebral slices when NA levels in the bathing medium were varied or agents which affect tissue Na content were added. When NaCl was gradually replaced with Tris-HCl or choline chloride, cyclic AMP formation was progressively enhanced. When NA was below 30mM, cyclic AMP formation reached the maximum (approximately 30 fold), but this increment was not blocked by tetrodotoxin. The stimulatory effect of high K was nearly linear over 120mM and became much more prominent when NA was decreased to 30 to 40mM in the bathing medium. The effect of high K also was not blocked by tetrodotoxin. Ouabain, electrical impluses and glutamate each stimulated cyclic AMP formation about 17 fold, 7 fold, and 5 fold, respectively. Tetrodotoxin completely blocked the effects of electrical pulses and partially

blocked the effects of glutamate and ouabain. It is suggested that the increase of cyclic AMP in cerebral cortical slices may be related to the decrease in NA gradient across the cell membrane. 27 references. (Author abstract)

002325 Young, John K.; Nance, Dwight M.; Gorski, Roger A. Department of Anatomy and Brain Research Institute, University of California, Los Angeles, CA 90024 **Effects of estrogen upon hypothalamic vulnerability to goldthioglucose in mice.** Brain Research Bulletin. 3(3):231-235, 1978.

The effects of estrogen treatment on the glucoreceptive function of the ventromedial hypothalamus in mice, as indexed by the extent of hypothalamic lesions following a systemic injection of goldthioglucose (GTG), were examined. Two groups of ovariectomized albino mice were given subcutaneous injections of either sesame oil or increasing doses of estradiol benzoate (EB) for 8 days. Mice were housed in groups of three; food intake (FI) and bodyweight (BWT) were injected intraperitoneally with 0.3mg/g of GTG and sacrificed 2 days later. The extent of hypothalamic damage after GTG was assessed histologically. Although EB did not depress FI or BWT, perhaps because of some behavioral interaction within the groups of mice, the extent of hypothalamic damage after GTG was significantly increased in EB treated mice relative to that of oil injected controls. Data support the view that estrogen may enhance the uptake and/or storage of glucose by the ventromedial hypothalamus. 50 references. (Author abstract)

002326 Zahlava, J.; Sobotka, P. Institute of Pathophysiology, Medical Faculty, Charles University, Lidicka 1,Plzen, Czechoslovakia **Changes of the electrical activity in cortical auditory areas produced by penicillin.** Activitas Nervosa Superior (Praha). 20(2):106-107, 1978.

In a paper presented at the 14th Interdisciplinary Conference on the Experimental and Clinical Study of Higher Nervous Functions held at Marianske Lazne, Czechoslovakia, in October 1977, a study examining changes of the electrical activity in cortical auditory areas of dogs and rats produced by penicillin (PNC) was reported. The spontaneous and evoked cortical activity was recorded in 18 male rats and in 10 pups in two cortical auditory areas: g. ectosylvius anterior and medius. EEG was recorded either 30 minutes after a single application in dogs and for several hours in rats to which PNC was applied repeatedly in 30 minute intervals. In rats the epileptogenic seizure activity appeared 5 to 30 minutes after the application. In dogs the focus of the spontaneous epileptogenic activity was very steady and persisted some hours after the application. It is concluded that the different changes of cortical auditory potentials in dogs confirmed the functional independence of both cortical auditory areas. 3 references.

002327 Zarifian, E. Centre Hospitalier Sainte-Anne, 1, rue Cabanis, F-75674 Paris Cedex 14, France **/Anxiolytic medications and inhibition./** Medicaments anxiolytiques et inhibition. Encephale (Paris). 4(5, Supplement):547-551, 1978.

In a paper presented at the Conference on the Concept of Inhibition in Psychiatry, held in Monastir, Yugoslavia, October 1978, the different meanings of the term disinhibition in psychopharmacology and psychiatry are discussed. The action of antianxiety agents on animal behavior is described with emphasis on the passive and active avoidance tests. The mode of action and site of action of benzodiazepines are also considered, with focus on the existence of an endogeneous ligand displacing the binding of diazepam. The differences between low and high doses of antianxiety agents are stressed in patients and normal volunteers, and the treatment of inhibition by benzodiazepines is also discussed. 10 references. (Journal abstract modified)

002328 Zieglgansberger, W.; Tulloch, I. F. Max-Planck-Institut fur Psychiatrie, Department of Neuropharmacology, Kraepelinstrasse 2, D-8000, Munich 40, Germany **Effects of substance-P on neurones in the dorsal horn of the spinal cord of the cat.** Brain Research (Amsterdam). 166(2):273-282, 1979.

The effects of microiontophoretic application of synthetic substance-P and the active fragment, substance-P(4-11), on the activity of single neurons in the dorsal horn of the cat spinal cord were investigated using intracellular and extracellular recording techniques. In the majority of dorsal horn neurons studied, substance-P and substance-P(4-11) caused a slow and prolonged increase of the spontaneous firing rate and/or an enhancement of L-glutamate-induced activity. Intracellular studies indicated that substance-P caused a reversible depolarization of dorsal horn neurons and motoneurons, without a detectable alteration of the membrane resistance, antidromic action potential, or postsynaptic potentials. These results are compatible with the proposed role of substance-P in sensory transmission in the cat spinal cord. 50 references. (Author abstract modified)

04 MECHANISM OF ACTION: BEHAVIORAL

002329 Adam-Carriere, Dyane; Merali, Z.; Stretch, Roger. Faculty of Psychology, University of Ottawa, Ottawa, Ontario Canada K1N 6N5 **Effects of morphine, naloxone, d,l-cyclazocine, and d-amphetamine on behaviour controlled by a schedule of interresponse time reinforcement.** Canadian Journal of Physiology and Pharmacology (Ottawa). 56(5):707-720, 1978.

The separate effects of graded doses of morphine, naloxone, d,l-cyclazocine, and d-amphetamine on responding maintained by differential reinforcement of low rate schedule (DRL) of food presentation were examined in rats. Cyclazocine, as well as morphine, produced dose dependent decreases in the number of reinforcements per session. d-Amphetamine exerted a biphasic effect on responding; small doses increased response rates and large doses suppressed responding. Naloxone at otherwise inactive doses was found to antagonize the rate decreasing effects of morphine and to reduce the rate increasing effects of d-amphetamine. It is noted that few experiments have dealt previously with the development of tolerance to the behavioral effects of morphine under comparable dose regimens, time course relationships, or behavioral testing procedures. Systematic analyses of these interrelated variables are needed since it is evident that schedules employed to maintain responding itself exerts significant effects. 32 references. (Author abstract modified)

002330 Adkins, Elizabeth K.; Pniewski, Ellen E. Dept. of Psychology, Uris Hall, Cornell University, Ithica, NY 14853 **Control of reproductive behavior by sex steroids in male quail.** Journal of Comparative and Physiological Psychology. 92(6):1169-1178, 1978.

For the purpose of elucidating the biochemical mechanisms by which androgens activate male reproductive behavior in Japanese quail, two experiments were conducted that examined the ability of different sex steroids to stimulate crowing, strutting, and copulation. Results suggest that copulation in quail may involve conversion of testosterone to estrogen by the brain, that crowing and strutting may involve conversion of testosterone to dihydrotestosterone by the brain, and that in quail, the different components of male reproductive behavior show divergent patterns of hormone responsiveness. Thus, the neural tissues underlying these behaviors have different molecular requirements for activation by steroids. 42 references. (Author abstract modified)

002331 Aigner, Thomas G.; Balster, Robert L. Department of Psychiatry, University of Chicago, Chicago, IL 60637 **Rapid substitution procedure for intravenous drug self-administration**

studies in rhesus monkeys. Pharmacology Biochemistry and Behavior. 10(1):105-112, 1979.

A rapid substitution procedure was developed for initial screening of drugs with potential reinforcement efficacy. Rhesus monkeys were trained to press a lever 100 times to obtain a food pellet or an intravenous drug injection. Two daily experimental sessions were divided into three 15 minute periods each; in periods 1 and 3 lever-pressing was maintained by the delivery of food, while period 2 responding was maintained by iv injection of a drug solution. The drug available each followed a 4 day sequence of cocaine (30mcg/kg/injection), saline, cocaine, and test compound. Morphine, oxymorphine, codeine, pentazocine, d-amphetamine, and methylphenidate all maintained period 2 responding at rates significantly greater than saline. Cyclazocine, naloxone, levallorphan, scopolamine, chlorpromazine, fenfluramine, and (●)-9-nor-9-alpha-hydroxy-hexahydrocannabinol (alpha-HHC) did not maintain responding during period 2. The results with procaine, beta-HHC, and nalorphine were equivocal. 25 references. (Author abstract modified)

002332 Amir, S.; Solomon, M.; Amit, Z. Center for Research on Drug Dependence, Concordia University, 1455 de Maisonneuve Blvd. W., Montreal, Quebec, Canada, H3G 1M8 **The effect of acute and chronic naloxone administration on motor activation in the rat.** Neuropharmacology (Oxford). 18(2):171-173, 1979.

The acute and chronic effects of naloxone on motor activity were studied in male Wistar rats. No difference in motor activity was noted between naloxone treated (2.5, 5.0, and 10.0mg/kg ip) and saline treated rats on the first day of testing. However, all three doses of naloxone blocked the increase in motor activation seen in the saline treated animals upon repeated testing. Results suggest that endogenous opioid peptide systems may play a role in behavioral activation and adaptation. 22 references. (Author abstract modified)

002333 Andrews, C. D.; Woodruff, G. N. Department of Physiology and Pharmacology, University of Southampton, Southampton, England **Effect of the ()- and (-)-enantiomers of sulpiride on ADTN-induced hyperactivity in the rat.** British Journal of Pharmacology (London). 64(3):434P, 1978.

In a paper presented at the September 1978 meeting of the British Pharmacological Society at the University of Nottingham, the effects of the ()- and (-)-enantiomers of sulpiride on hyperactivity induced by 2-amino-6,7-dihydroxy-1,2,3,4-tetrahydronaphthalene (ADTN) in rats are reported. Bilateral injection of ADTN into the nucleus accumbens caused a potent, dose related stimulation of locomotor activity. Intraperitoneal injection of fluphenazine (0.2mg/kg) completely blocked the response to ADTN. Intraperitoneal ()-sulpiride was much less active, causing complete abolition of ADTN-induced locomotor stimulation at a dose of 20mg/kg and only partial inhibition at a dose of 10mg/kg. In contrast, following bilateral injection into the nucleus accumbens, sulpiride was extremely potent in blocking the action of ADTN, the (-)-enantiomer being about 25 times more active than the ()-enantiomer. Neither naloxone nor metoclopramide caused significant attenuation of the ADTN response when similarly applied. 3 references. (Author abstract modified)

002334 Anlezark, G. M.; Horton, R. W.; Meldrum, B. S. Dept. of Neurology, Institute of Psychiatry, Denmark Hill, London, SE5 8AF, England **Dopamine agonists and reflex epilepsy.** Advances in Biochemical Psychopharmacology. 19:383-388, 1978.

The effects of drugs that act as direct or indirect dopamine (DA) agonists were tested in two models of reflex epilepsy, audiogenic seizures in DBA/2 mice and photically-induced seizures in the Senegalese baboon Papio papio. The drugs used included the DA agonists apomorphine and n-N-propylnorapomorphine; the ergot alkaloids ergocornine, bromocriptine, ergometrine, and lysergic acid diethylamide; and the 5-hydroxytryptamine (5-HT) agonist quipazine. Results indicate that different anatomical pathways are involved in the mediation of seizure activity in the two models. The drugs appeared to reduce audiogenic seizure susceptibility primarily through their DA agonist activity and to inhibit reflex epilepsy in the baboon via interaction with central 5-HT receptors. 17 references.

002335 Arnt, J.; Christensen, A. V.; Scheel-Kruger, J. Psychopharmacological Research Laboratory, Sct. Hans. Mental Hospital, DK-4000 Roskilde, Denmark **Benzodiazepines potentiate GABA-dopamine stereotyped dependent gnawing in mice.** Journal of Pharmacy and Pharmacology (London). 31(1):56-58, 1979.

The effects of a series of benzodiazepines on dopamine/gamma-aminobutyric acid dependent stereotyped gnawing in mice were examined. In low doses, the benzodiazepines potentiated the effect of muscimol on methylphenidate-induced stereotyped gnawing; their rank order of potency in this respect corresponds to their comparative affinity for the specific benzodiazepine receptor. In the absence of muscimol, the benzodiazepines induced only a moderate increase in methylphenidate-induced gnawing, reaching only 20-50% of the maximum score even after extremely high doses. In contrast to muscimol, the benzodiazepines increased methylphenidate-induced locomotor activity. 25 references.

002336 Arushanyan, E. B.; Tolpyshev, B. A. Kafedra farmakologii Chitinskogo meditsinskogo instituta, Chita, USSR /**The influence of clozapine on behavioral and electrographic indices of the arrest function of the caudate nucleus in cats.**/ Vliyaniye klozapina na povedencheskiye i elektrograficheskiye pokazateli zaderzhivayushchey funktsii khvostatogo yadra u koshek. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 85(5):541-544, 1978.

Twenty two cats were used in a series of experiments to observe the effects of clozapine on the functioning of the caudate nucleus. The drug was administered in increasing doses (1-5mg/kg) to the animals while they were in an unrestrained state. This was found to cause a behavioral depression and the suppression of amphetamine-induced stereotypy of behavior against a background of marked vegetative shifts. Clozapine, like chlorpromazine, intensified the behavioral (arrest reaction) and electrographic (neocortical caudate spindle) indices of the caudate nucleus' functioning. Arrest reaction was found to change more distinctly with stimulation of the ventral parts of the nucleus head. 13 references. (Journal abstract modified)

002337 Ashley, David V. M.; Coscina, Donald V.; Anderson, G. Harvey. Dept. of Nutrition and Food Science, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada **Selective decrease in protein intake following brain serotonin depletion.** Life Sciences (Oxford). 24(11):973-984, 1979.

The effect of reduced brain serotonin (5-HT) concentration on protein and calorie intake was investigated in young male Wistar rats given access to isocaloric 15% and 55% casein diets in two food cups. Systemic administration of p-chlorophenylalanine, central administration of 5,7-dihydroxytryptamine, or lesions of the midbrain raphe resulted in 20 to 30% reductions in the amount of protein consumed over a 2 week period, with no change in the total caloric intake. The decrease in the proportion of dietary energy selected as protein was associated with a reduction in brain 5-HT and 5-hydroxyindoleacetic acid. Results support previous work implicating brain 5-HT metabolism in the

selective control of protein intake. 38 references. (Author abstract modified)

002338 Baraldi, M.; Benassi-Benelli, A.; Bernabei, M. T.; Cameroni, R.; Ferrari, F.; Ferrari, P. Institute of Pharmacology, University of Modena, Via G. Campi 287, Modena, Italy **Apocodeine-induced stereotypies and penile erection in rats.** Neuropharmacology (Oxford). 18(2):165-169, 1979.

Small doses of apocodeine (APC) increased spontaneous penile erection (PE) in adult Wistar rats in a dose related manner for doses up to 50mcg/kg ip; larger doses were progressively less active. APC evoked stereotyped behavior (SB) in these animals only at doses of 10mg/kg or larger. Oral administration of APC induced PE, but did not induce SB at any dose. The behavioral effects of APC in rats were similar to those produced by apomorphine, and both drugs acted on central dopamine receptors. PE and SB appear to be mediated by functionally distinct mechanisms. 24 references. (Author abstract modified)

002339 Bartus, Raymond T. CNS Research Section, Medical Research Division, American Cyanamid Co., Pearl River, NY 10965 **Short-term memory in the Rhesus monkey: effects of dopamine blockade via acute haloperidol administration.** Pharmacology Biochemistry and Behavior. 9(3):353-357, 1978.

The effects of dopaminergic blockade on recent or short-term memory (STM) were evaluated in test sophisticated Rhesus monkeys tested under several doses of the antidopaminergic haloperidol (0.006 to 0.05mg/kg) in an automated delayed response procedure. This procedure had previously demonstrated profound STM impairments in aged monkeys and strikingly similar deficits in young monkeys given the anticholinergic scopolamine. Results did not support the notion that dopaminergic mechanisms are critical in primate STM. Although significant impairments in delayed response accuracy were observed with higher haloperidol doses, they were unrelated to the duration of the retention interval, implying a more general nonmnemonic dysfunction. Since the qualitative nature of this deficit is dissimilar to, and not as specific as, that previously found in aged Ss or young Ss given scopolamine, it is suggested that age related changes observed in the dopaminergic system are less likely to be responsible for the aged STM impairments than comparable age related changes in the cholinergic system. 28 references. (Author abstract modified)

002340 Bean, Noel Jay; Conner, Robert. Department of Psychology, Bowling Green State University, Bowling Green, OH 43403 **Central hormonal replacement and home-cage dominance in castrated rats.** Hormones and Behavior. 11(1):100-109, 1978.

The effect of central placement of gonadal hormones on reinstating home cage dominance behaviors in castrated rats was studied. Following the placement of testosterone or estradiol into the preoptic area of castrated rats, some dominance behaviors were reinstated to precastration levels, while neither hormone implants into the septum nor cholesterol implants into either the preoptic or septal areas produced any reliable effects. 31 references. (Author abstract)

002341 Bedford, John A.; Bailey, Lillian P.; Wilson, Marvin C. Research Institute of Pharmaceutical Sciences, School of Pharmacy, University of Mississippi, University, MS 38677 **Cocaine reinforced progressive ratio performance in the rhesus monkey.** Pharmacology Biochemistry and Behavior. 9(5):631-638, 1978.

A series of experiments conducted to determine the effectiveness of a progressive ratio (PR) procedure in measuring the relative reinforcing efficacy of several intravenous doses of cocaine is described. In experiment 1, utilizing much smaller increases in the ratio requirement than previously reported, the animals generally displayed increases in breaking point with increases in the cocaine unit dose up to 0.4mg/kg/inj. The highest does studied (0.8mg/kg/inj.)engendered breaking points lower than the 0.4mg/kg dose but higher than the remaining lower doses. Experiment 2 used the same reinforcement schedule as in experiment 1 but with liquid Tang as the reward. Results demonstrate that this procedure would function to discriminate reinforcing strength with a more traditional reward. 14 references. (Author abstract modified)

002342 Beninger, Richard J.; Phillips, Anthony G. Department of Psychology, University of British Columbia, Vancouver, BC, Canada V6T 1W5 **Possible involvement of serotonin in extinction.** Pharmacology Biochemistry and Behavior. 10(1):37-41, 1979.

Rats trained to lever-press for continuous reinforcement with food were intubated with the serotonin synthesis inhibitor p-chlorophenylalanine (PCPA, 400mg/kg) or water. The PCPA-treated rats responded at a higher rate than control rats during extinction sessions, and this increased responding did not appear to be related to a general elevation in activity. In a second experiment with rats trained on a random interval schedule prior to treatment with PCPA or water, there was no significant difference in the resistance to extinction of the two groups. In a third experiment with rats trained in a punished step down a response paradigm the responses of rats treated with PCPA took longer to recover than water injected controls. Results suggest that serotonergic neurons may play a role in extinction processes. 17 references. (Author abstract modified)

002343 Bhakthan, N. M. G.; Chiu, S. Dept. of Kinesiology, Simon Fraser University, Burnaby, British Columbia V5A 1S6, Canada **Deranged diurnal feeding pattern and altered brain serotonin turnover in heroin-dependent rats.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 235(2):289-298, 1978.

The effects of heroin tolerance and dependence on diurnal feeding and brain serotonin turnover were examined in rats. Rats administered escalating dosages of heroin from 5mg/kg-1 to 30mg/kg-1 twice daily for 10 days exhibited disrupted diurnal feeding patterns: daylight food intake increased significantly, while night food intake decreased significantly. Growth rate was also considerably attenuated. Heroin treated rats showed typical abstinence signs upon naloxone challenge 8 hours after last heroin challenge. No significant changes were observed in brain levels of tryptophan, serotonin, or 5-hydroxyindoleacetic acid. Labeled serotonin from labeled tryptophan was significantly reduced as evidenced by the decreased specific activity of serotonin. It is concluded that while the disturbed diurnal feeding cannot be exclusively ascribed to altered serotonergic mechanism, chronic heroin treatment appears to effect a decrease in serotonin rate via a negative feedback loop. 24 references. (Author abstract modified)

002344 Bissette, G.; Nemeroff, C. B.; Loosen, P. T.; Breese, G. R.; Burnett, G. B.; Lipton, M. A.; Prange, A. J., Jr. Biological Sciences Research Center, University of North Carolina, Chapel Hill, NC 27514 **Modification of pentobarbital-induced sedation by natural and synthetic peptides.** Neuropharmacology (Oxford). 17(4/5):229-237, 1978.

The effect of intraperitoneal (ip) and intracisternal (ic) injection of 47 endogenous peptides and related analogues on the sedation produced by sodium pentobarbital (55mg/kg ip) in male Swiss-Webster mice was examined. Several peptides antagonized the effects of pentobarbital, but only one (neurotensin) markedly potentiated them. Certain peptides were active only after ic in-

jection, while others were effective by either route of administration; peptides active after ip administration were always active after ic administration. Thyrotropin releasing hormone was the most effective antagonist and was active by both routes. Neurotensin was the most potent potentiator, but was active only after central administration. Although few general structural requirements for analeptic activity of peptides were discernable, it appears that such activity is mediated by the central nervous system. 31 references. (Author abstract)

002345 Blackman, D. E.; Sanger, D. J. Department of Psychology, University College, Cardiff CF1 1XL, Wales **Contemporary research in behavioral pharmacology.** New York, Plenum, 1978. 506 p. $32.50.

Evaluative reviews of behavioral pharmacological research are presented. Topics discussed include: schedule controlled behavior and the effects of drugs, the effects of drugs on behavior controlled by aversive stimuli, continuous avoidance procedures, the conditioned emotional response, stimulus control and drug effects, drug-induced stimulus control, the effects of drugs on adjunctive behavior, schedule-induced self-administration of drugs, drugs as reinforcers, behavioral tolerance, and behavioral toxicology.

002346 Blair, R.; Liran, J.; Cytryniak, H.; Shizgal, P.; Amit, Z. Center for Research on Drug Dependence, Concordia University, 1455 de Maisonneuve Blvd. W., Montreal, Quebec H3G 1M8, Canada **Explosive motor behavior, rigidity and periaqueductal gray lesions.** Neuropharmacology (Oxford). 17(3):205-209, 1978.

To examine the relationship between explosive motor behavior (EMB), rigidity, and the periaqueductal gray (PAG), the effects of intraventricularly administered morphine and etonitazene were compared in PAG lesioned and nonlesioned rats. Lesioned animals exhibited EMB shortly after surgery; however, when tested 24 hours postsurgery they failed to exhibit the usually observed EMB in response to an intraventricular infusion of morphine. In contrast, lesioning did not interfere with the ability of intraventricularly infused etonitazene to produce rigidity. Results suggest that the site of action for morphine-induced EMB is the PAG and that the neural substrate for EMB and rigidity are, at least in part, anatomically distinct. 8 references. (Author abstract modified)

002347 Bodnar, Richard J.; Kelly, Dennis D.; Spiaggia, Angela; Pavlides, Constantine; Glusman, Murray. Department of Behavioral Physiology, New York State Psychiatric Institute, 722 West 168th Street, New York, NY 10032 **Stress-induced analgesia: effect of naloxone following cold water swims.** Bulletin of the Psychonomic Society. 12(2):125-128, 1978.

The effect of naloxone on stress-induced analgesia in rats was investigated. It is asserted that rats exposed to novel stressful events subsequently display increased nociceptive thresholds while chronic exposure produces adaptation. Naloxone at a dose of 10 mg/kg was partially able to attenuate stress-induced analgesia following a forced cold water swim but it had no effect upon normal nociceptive thresholds in unstressed control subjects. The data suggest that stress-induced analgesia is not identical to that induced by opiates. 32 references. (Author abstract modified)

002348 Boland, Frederick Joseph. McGill University, Canada **Suppression by lithium of voluntary alcohol ingestion in the rat. (Ph.D. dissertation).** Dissertation Abstracts International. 39(4):1943-B, 1978.

To examine mechanisms, through which lithium suppresses voluntary alcohol ingestion, four experiments were conducted on 70 rats showing a low to moderate preference for aversive alcohol solutions or a high preference induced by hypothalamic stimulation. In Experiments 1 and 2, lithium injection suppressed alcohol ingestion only if alcohol was tested. Pairing lithium contiguously with water or intubed alcohol failed to reduce subsequent alcohol ingestion, despite the presence of high serum lithium levels. In Experiments 3 and 4, a series of seven lithium injections increased rather than decreased alcohol intake if lithium was allowed to accumulate in blood and brain during alcohol exposure while the transitory sickness associated with injection was prevented from being associated with the taste of alcohol. Results suggest that lithium effects are the result of a learned taste aversion, rather than a pharmacological mechanism specific to alcohol. (Journal abstract modified)

002349 Bourn, W. M.; Chin, L.; Picchioni, A. L. School of Pharmacy, Northeast Louisiana University, Monroe, LA 71209 **The role of dopamine in sound-induced convulsions.** Journal of Pharmacy and Pharmacology (London). 30(12):800-801, 1978.

To determine the role of dopamine in audiogenic seizures, audiogenic response scores (ARS) were obtained in female rats treated with 6-hydroxydopamine (6-OHDA), desipramine, or both. Desipramine alone produced no significant change in brain catecholamine concentrations or in ARS. The 6-OHDA treatment significantly reduced noradrenaline concentrations in all brain regions examined; significantly reduced dopamine in the cortex, striatum, and hypothalamus; and significantly decreased ARS. In rats pretreated with desipramine prior to 6-OHDA, a significant decrease in dopamine concentration in the cortex and striatum was observed, but no depletion of noradrenaline and no significant changes in ARS were found. Results indicate that dopamine is not a significant factor in the inhibitory modulation of audiogenic seizures. 14 references.

002350 Bouyer, Jean-Jacques; Dedet, Laure; Debray, Odile; Rougeul, Arlette. Laboratoire de Neurophysiologie comparee, Universite P. & M. Curie, F-75005 Paris, France **Restraint in primate chair may cause unusual behavior in baboons; electrocorticographic correlates and corrective effects of diazepam.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 44(5):562-567, 1978.

The electrocorticographic (ECoG) correlates and effects of diazepam on the unusual behavior caused in baboons by restraint in a primate chair were studied. Unusual behavior included closed eyes and only slight reaction to the approach of the experimenter (opening of the eyes), in contrast with their active behavior when left free to move about in the cage. When the ECoG was recorded from certain cortical areas (particularly somatic area I), an unusual pattern developed during the restrained state: rhythms which typically appear during the transition from wakefulness to sleep developed in long sustained sequences. Administration of diazepam caused both the behavior and the ECoG of the restrained animal to return to normal. The unusual behavior and ECoG observed may have been a stress reaction to the restraint. 13 references. (Author abstract modified)

002351 Breese, George R.; Mueller, Robert A.; Hollister, Alan; Mailman, Richard. Biological Sciences Research Center, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Importance of dopaminergic pathways and other neural systems to behavior and action of psychotropic drugs.** Federation Proceedings. 37(10):2429-2433, 1978.

At the Annual Fall Meeting of the American Society for Pharmacology and Experimental Therapeutics held in Columbus, August 23, 1977, a paper was presented in which evidence linking certain behaviors and functions with synaptic transmis-

sions of dopaminergic pathways in the central nervous system is summarized. The role of dopaminergic mechanisms in the pharmacology of centrally acting drugs is discussed. Neural circuits that modulate and compensate for alterations in dopaminergic neural function are elucidated. It is concluded that dopaminergic fibers are clearly implicated in behavior and in the actions of psychotropic drugs, but definition of the mechanisms by which dopaminergic fibers induce these changes remains elusive. 43 references.

002352 Brien, James F.; Kitney, John C.; Peachey, John E.; Rogers, Beverley J. Addiction Research Foundation, Queen's University, Kingston, Canada K7L 3N6 **Methamphetamine-induced behavioural effects and brain concentrations of methamphetamine and its metabolite amphetamine in mice.** Research Communications in Chemical Pathology and Pharmacology. 22(2):313-328, 1978.

The correlations between brain concentrations of methamphetamine and its metabolite amphetamine and methamphetamine-induced behavior effects were investigated in mice. Increasing doses of methamphetamine produced decreased quiescence, increased locomotor activity, and stereotyped behavior. During the 90 min experimental period, there was no positive correlation between the magnitude of each type of drug-induced behavior and the brain methamphetamine concentration. Amphetamine appears to have only a small involvement in the methamphetamine-induced behavioral effects. 17 references. (Author abstract modified)

002353 Broadhurst, P. L. no address **Drugs and the inheritance of behavior: a survey of comparative psychopharmacogenetics.** New York, Plenum, 1978. 206 p. $19.50.

The tools of behavior/genetic analysis are employed to reveal the genetic architecture of the drug-induced phenotypes. An exhaustive review of the literature on the subject is provided. Strain and species differences in response to amphetamine and other stimulants, to nicotine, anxiolytics, convulsants, and amnesics, and to alcohol, opiates, and barbiturates are covered. Selection, diallel crossbreeding, and the use of recombinant inbred strains are described and the ways in which these techniques have been used in areas relevant to pharmacogenetics are discussed. More research using each of these techniques is recommended and suggestions are made of ways of maximizing the information gained from future studies.

002354 Brown, K. Dept. of Psychology, Queen's University of Belfast, Belfast, Northern Ireland **Signal detection analysis of drug effects.** Irish Journal of Medical Science (Dublin). 147(Supplement 1):10-13, 1978.

A paper read at the first Irish Psychopharmacology Conference, held in Belfast in March 1978, is presented. A technique based on signal detection or statistical decision theory is described. This technique was applied to the analysis of the effects of the cholinergic drugs, scopolamine and physostigmine, on performance in a discrimination learning task. A series of peripheral injection studies is discussed and it is suggested that the drug effects are consistent with the view that cholinergic processes in the central nervous system are involved in the modulation of stimulus selection or attention. A study in which the same drugs were injected into dorsal and ventral hippocampal sites is described. 15 references. (Author abstract modified)

002355 Buhl, A. E.; Jensen, J. N.; Phoenix, C. H. Oregon Regional Primate Research Center, 505 Northwest 185th Ave., Beaverton, OR 97005 **Influence of progesterone on sexual behavior in castrated male rhesus monkeys treated with testosterone.** Hormones and Behavior. 10(3):258-263, 1978.

The effect of progesterone on sexual behavior was tested in five long-term castrated rhesus monkeys treated simultaneously with testosterone and progesterone. A control group consisting of three long-term castrates was treated only with testosterone. Plasma levels of testosterone and progesterone were measured at weekly intervals, and behavioral data were collected for each animal twice weekly throughout the study. Progesterone has been reported to inhibit sexual behavior in male guinea-pigs and mice, but results from 8 weeks of testing show that levels of behavior in both groups of monkeys did not differ. 18 references. (Author abstract)

002356 Cameron, William Ritchie. Texas Christian University **The influence of the hippocampus on feminine sexual behavior: dorsal-ventral distinctions. (Ph.D. dissertation).** Dissertation Abstracts International. 39(6):3033-B, 1978. Ann Arbor, Univ. Microfilms No. 7822288, 144p., 1978.

The influence of the hippocampus on feminine sexual behavior was investigated via bilateral radio frequency lesions of the dorsal or ventral hippocampus of ovariectomized rats and administration of various doses of progesterone and estrogen. Ss which sustained damage to the dorsal hippocampus displayed a lower probability and intensity of lordotic behavior than controls on both preprogesterone and postprogesterone tests. Lesions of the ventral hippocampus tended to have a significant facilitatory effect on LQ scores and heightened the lordotic intensity scores in both tests. (Journal abstract modified)

002357 Carroll, Marilyn E.; Meisch, Richard A. Psychiatry Research Unit, Mayo Box 392, University of Minnesota, Minneapolis, MN 55455 **Effects of food deprivation on etonitazene consumption in rats.** Pharmacology Biochemistry and Behavior. 10(1):155-159, 1979.

The effects of food deprivation on etonitazene intake in male Wistar rats given continuous access to the drug in their drinking water were examined. Free feeding rats given a 5mcg/ml etonitazene hydrochloride solution as their sole liquid increased their drug intake by 100% when they were partially food deprived for 23 days. A second drug group that remained food satiated did not show similar increases in drug intake, but drank greater volumes of the etonitazene solution than a food satiated control group drank of water. A fourth group showed a 50% decrement in water intake during similar food deprived conditions. During a second food deprivation phase, large increases in drug intake occurred almost immediately, compared with a gradual increase over 17 days during the first food deprivation phase, suggesting the involvement of a learning mechanism. Self-mutilation and other forms of stereotypy were observed only in food deprived, etonitrazene treated rats. 32 references. (Author abstract modified)

002358 Cascione, Rosa. Duke University **Influence of brain monoamines on the courtship behavior of male ring doves (Streptopelia risoria). (Ph.D. dissertation).** Dissertation Abstracts International. 39(5):2560-B, 1978. Ann Arbor, Univ. Microfilms No. 7821298, 81p., 1978.

To determine whether brain monoamines are involved in regulation of courtship behavior, and to elucidate the physiological nature of and any monoaminergic effects, male ring doves received intracerebral implants of various pharmacological agents. Results show that L-norepinephrine, d-norepinephrine, phenylephrine, isoproterenol, tyramine, serotonin, p-chlorophenylalanine, barium chloride, and papaverine, effectively suppress the bow cooing and nest soliciting courtship displays when placed within a circumscribed ventromedial forebrain region having the preoptic/anterior hypothalamic area as its approximate center. Courtship displays are little or not suppressed by desi-

pramine, dopamine, alpha-methyl-p-tyrosine, phentolamine, LB 46, gamma-amino-butyric acid, glutamic acid. Although nonspecific drug effects may account for a large degree of observed behavioral suppression, differential effectiveness of drugs on bow cooing and nest soliciting suggests that nets soliciting is specifically inhibited by an alpha-adrenergic neural system located within the preoptic/anterior hypothalamic brain area. (Journal abstract modified)

002359 Chapman, Robert H.; Stern, Judith M. Stern: Dept. of Psychology, Rutgers College, Rutgers University, New Brunswick, NJ 08903 **Maternal stress and pituitary-adrenal manipulations during pregnancy in rats: effects on morphology and sexual behavior of male offspring.** Journal of Comparative and Physiological Psychology. 92(6):1074-1083, 1978.

The demasculinizing and feminizing effects of prenatal stress (i.e.,stress applied to the mother during pregnancy) in rats was investigated to determine whether such effects are mediated by activation of the maternal pituitary-adrenal axis. Neither whole body restraint, with or without hyperthermia, nor adrenocorticotrophic hormone treatment during the last third of gestation had any reliable effect on masculine or femine sexual behavior in male Sprague-Dawley offspring, although these treatments produced maternal pathology and evidence of maternal adrenocorticoid release. Significant littermate similarity was found for almost every morphological and behavioral measure. Failure to control for the litter variable may account for many previously reported effects of prenatal stress on sexual behavior in rats. 36 references. (Author abstract modified)

002360 Clemens, Lynwood G.; Gladue, Brian A. Dept. of Zoology, Michigan State University, East Lansing, MI 48824 **Feminine sexual behavior in rats enhanced by prenatal inhibition of androgen aromatization.** Hormones and Behavior. 11(2):190-201, 1978.

The enhancement of feminine sexual behavior in rats by prenatal inhibition of androgen aromatization was investigated. Male and female rats were exposed to the aromatization inhibitor 1,4,6-androstatriene-3,17-dione (ATD) in utero via prenatal injections to the pregnant mother. In adulthood, lordosis behavior was measured in response to ovarian hormones. Males and females exposed prenatally to ATD showed enhanced lordosis behavior in response to estrogen alone and in response to estrogen plus progesterone when compared to controls. These data lend further support to the idea of a prenatal, androgen sensitive phase of sexual differentiation in which defeminization normally occurs in both male and female rats. Further, these data support the concept that androgen aromatization is an important process in this defeminization. 31 references. (Author abstract modified)

002361 Clemens, Lynwood G.; Popham, Teresa V.; Ruppert, Patricia H. Department of Zoology, Michigan State University, East Lansing, MI 48824 **Neonatal treatment of hamsters with barbiturate alters adult sexual behavior.** Developmental Psychobiology. 12(1):49-59, 1979.

The effects of 50mg pentobarbital, 100mg pentobarbital, or 100mg d-amphetamine at day 2 to 4 on the adult sexual behavior of male and female golden hamsters were examined. When tested for masculine sexual behavior in adulthood, males treated with 100mg pentobarbital showed behavioral deficits. Deficits shown by 50mg pentobarbital males were overcome by testosterone replacement. Males treated with amphetamine showed no differences from controls when tested for sexual behavior. Drug treatments had no effect on adult sexual behavior in neonatally treated females. It is concluded that pentobarbital can inhibit normal masculinization of the male hamster when given during behavioral sexual differentiation. 28 references. (Author abstract modified)

002362 Contreras, E.; Tamayo, L.; Quijada, L. Dept. of Pharmacology, University of Concepcion, Concepcion, Chile **Partial inhibition of the abstinence syndrome in morphine tolerant-dependent mice following pharmacological denervation.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 235(1):124-133, 1978.

The effects of chronic blockade of cholinergic and serotonergic receptors on physical dependence and tolerance to morphine was examined in mice. Pretreatment with varios doses of atropine or methysergide for 6 days prior to injection of a slow release morphine preparation had no affect on the intensity of morphine tolerance, but partially reduced some manifestations of naloxone-induced abstinence behavior. The attenuation of the abstinence syndrome in pretreated mice was reversed by an additional dose of atropine or methysergide, administered a few minutes before naloxone. Chronic pretreatment with pentobarbital had no significant effect on morphine dependence and tolerance. Studies with physostigmine and 5-hydroxytryptophan in morphine dependent mice suggested that morphine physical dependence may be the manifestation of compensatory changes in sensitivity to serotonin and acetylcholine in the CNS. 25 references. (Author abstract modified)

002363 Cooper, S. J. Dept. of Psychology, Queen's University of Belfast, Belfast, Northern Ireland **Benzodiazepines: relations between their effects on feeding and on anxiety.** Irish Journal of Medical Science (Dublin). 137(Supplement 1):14-18, 1978.

A paper read at the first Irish Psychopharmacology Conference, held in Belfast in March 1978, is presented. Findings on the effects of benzodiazepines upon feeding and anxiety are discussed. Clinically, benzodiazepines relieve anxiety. In animal experiments, they have been shown to reduce fear, avoidance and conflict. The hyperphagic effect of these compounds has been relatively neglected. The first proposals to account for the hyperphagia suggested that any effect on feeding was related to the anxiolytic effect of the drugs. Later evidence, however, has raised the possibility that the effect of benzodiazepines on feeding can be relatively direct and independent of a reduction in anxiety. Thus, primary and secondary hyperphagia can, in principle, be distinguished as mechanisms by which benzodiazepines affect feeding. 22 references. (Author abstract modified)

002364 Copenhaver, John H. University of Nebraska, Lincoln, NE 68508 **Serotonin depletion and aggressive behavior. (Unpublished paper).** Final Report, NIMH Grant R01-MH-27537, 1978. 8 p.

Three different modalities were tested as possible means by which brain levels of serotonin (5-hydroxytryptamine, 5-HT) could be lowered, thereby inducing a filicidal response in the female rodent where the behavior termed filicide is characterized by the lack of affective behavior prior to the aggressive attacking of a stimulus object, usually a 7-day-old pup, in the cervical/spinal area. None of the p-halogenated phenylalanines, p-chlorophenylethylamine (a possible metabolite of p-chlorophenylalanine (p-Cl-Phe), p-chloroamphetamine, or p-chloromethamphetamine compounds, which can reduce the levels of brain serotonin, were found to reliably induce a filicidal state. Although aggresive tendencies are in evidence prior to filicide, filicidal behavior becomes dominant once the whole brain level reaches a level of ca10mcg/g It is suggested that p-Cl-Phe reverses the normal protective behavior in the female animal by mediating the release of a natural latent aggressive tendency which is potentiated by the interference on, or reduc-

tion of, a suppressing system governed by serotonin. 10 references.

002365 Costall, B.; Funderburk, W. H.; Leonard, C. A.; Naylor, R. J. Funderburk: A. H. Robins Company Research Laboratories, 1211 Sherwood Avenue, Richmond, VA 23220 **Assessment of the neuroleptic potential of some novel benzamide, butyrophenone, phenothiazine and indole derivatives.** Journal of Pharmacy and Pharmacology (London). 30(12):771-778, 1978.

The neuroleptic action of benzamide, butyrophenone, phenothiazine, and indole derivatives was assessed in a series of behavioral tests in male Sprague-Dawley rats. Classical neuroleptics induced catalepsy alone or in combination with the acetylcholine-like agent RS86 or with alpha-methyl-p-tyrosine (alpha-MT); antagonized amphetamine induced stereotypy; and antagonized the hyperactivity induced by intraaccumbens or intrastriatal dopamine. In contrast, clozapine failed to interact with alpha-MT, and metoclopramide failed to antagonize mesolimbic hyperactivity or to interact with RS86. Clebopride, sultopride, tiapride, and N-(1-cyclohexyl-3-pyrrolidinyl)-2-methoxy-5-sulphamoyl benzamide (AHR6092) also failed to interact with RS86; clebopride was active in all other test situations, AHR6092 was inactive in all but an antiemetic test, sultopride was only weakly cataleptogenic, and tiapride only antagonized stereotypy and hyperactivity from the striatum. Other test compounds were inactive in catalepsy tests but exerted dopamine antagonistic potential in other test procedures. 14 references. (Author abstract modified)

002366 Costall, Brenda; Fortune, David H.; Naylor, Robert J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, West Yorkshire, England **Differential activities of some benzamide derivatives on peripheral and intracerebral administration.** Journal of Pharmacy and Pharmacology (London). 30(12):796-798, 1978.

The effects of metoclopramide, sultopride, celbopride, tiapride, and sulpiride on the hyperactivity induced by 1.5mg/kg ip amphetamine in male Sprague-Dawley rats were examined. Sulpiride failed to reduce amphetamine hyperactivity when administered peripherally (1-40mg/kg), but produced a dose dependent antagonism of the amphetamine effect when administered into the nucleus accumbens (1.25-5.0mcg). Tiapride had only a weak amphetamine antagonism when injected ip in doses up to 40mg/kg, but caused a marked, dose dependent antagonism of amphetamine when injected into the nucleus accumbens (0.31-1.25mcg). Metoclopramide, sultopride, and clebopride were active against amphetamine when administered by either route. Results suggest that the low efficacy of sulpride and tiapride following peripheral administration is related to a relative inability to penetrate the blood/brain barrier. 10 references.

002367 Cunha, Jomar M.; Masur, Jandira. Departamento di Psicobiologia, Escola Paulista de Medicina, Rua Botucatu, 862, 04023 Sao Paulo, Brazil **Evaluation of psychotropic drugs with a modified open field test.** Pharmacology (Basel). 16(5):259-267, 1978.

A modified open field test was developed for evaluating psychotrophic drugs. In the modified procedure, defecation scores were not considered. Rearing, grooming, and immobility were recorded, in addition to ambulation. The total time of observation was increased, and stimuli (light and sound) were presented separately rather than simultaneously. Results indicate that classes of psychotropic drugs can be differentiated on the basis of open field behavior, without taking defecation and grooming scores into consideration. In male Wistar rats, stimulants evoked a characteristic pattern of behavior, and neuroleptics could be differentiated from anxiolytics. Similarities between barbiturates and anxiolytics were detected. LSD produced a peculiar pattern of behavior, characterized by a marked reactivity to light. 12 references. (Author abstract modified)

002368 Cytawa, Jerzy; Jurkowlaniec, Edyta. Institute of Medical Biology, School of Medicine, Debinki 1, 80-211 Gdansk, Poland **Noradrenergic stimulation of the lateral hypothalamus as a reinforcement in T maze learning in rats.** Acta Neurobiologiae Experimentalis (Warszawa). 38(4):209-213, 1978.

The reinforcing properties of noradrenergic stimulation were studied in five male rats. The animals were permanently implanted with bilateral cannulas aimed at the perifornical region of the anterior part of the lateral hypothalamus. Once rats happened to go to the previously nonpreferred side of a T-maze and receive an injection of noradrenaline, they chose that side with increasing frequency in daily trials. This result demonstrates that noradrenaline-induced activation of the alimentary drive has an obvious reinforcing effect on motivated behavior. This effect is similar to that obtained in other experiments involving electrical stimulation of some brain areas. 25 references.

002369 D'Mello, G. D.; Stolerman, I. P. MRC Neuropharmacology Unit, Medical School, Birmingham B15 2TJ, England **Suppression of fixed-internal responding by flavour-amphetamine pairings in rats.** Pharmacology Biochemistry and Behavior. 9(3):395-398, 1978.

The possible effects of flavor amphetamine pairings on suppression of fixed interval (FI) responding were investigated in rats trained to press bars for water reinforcers delivered on a FI 1 min schedule. Flavored reinforcers were then substituted for the water and postsession injections of amphetamine (1mg/kg) were given. Even a single flavor amphetamine pairing produced some disruption of responding for the flavor, whereas three pairings almost completely suppressed responding. In the same Ss, flavors paired with saline injections did not suppress responding. Amphetamine (1mg/kg) injected before sessions of responding for plain water disrupted the temporal pattern of FI responding without affecting the total numbers of bar presses or the amounts of liquid consumed. Omitting primary reinforcement (water) throughout a single session also failed to suppress responding. The conditioned effects of the flavor were therefore different from the effects of either the unconditioned stimulus (amphetamine) or of an extinction procedure. 21 references. (Author abstract modified)

002370 Davis, H. L.; Johnson, D. D.; Crawford, R. D. Dept. of Pharmacology, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N OWO **Epileptiform seizures in domestic fowl. IX. Implications of the absence of anticonvulsant activity of ethosuximide in a pharmacological model of epilepsy.** Canadian Journal of Physiology and Pharmacology (Ottawa). 56(5):893-896, 1978.

Acute dose response studies were conducted to determine if ethosuximide had anticonvulsant activity against seizures evoked by stroboscopic stimulation of epileptic fowl and to correlate the observed effects with the concentration of the drug in the plasma. Ethosuximide, in doses that produced mean plasma concentration of 366 mcg/ml and signs of sedation, did not reduce seizure susceptibility. Twice daily administration of ethosuximide produced mean plasma concentrations of 430 mcg/ml after 36 hours without affecting seizure susceptibility even in the presence of marked sedation. Previous studies have shown that epileptic fowl are sensitive to the anticonvulsant effects of phenobarbital, phenytoin, and primidone at plasma concentrations similar to those required in humans. Since ethosuximide has a high specificity against petit-mal seizures in humans, the failure of ethosuximide to provide protection indicates that epileptic

fowl represent a relatively specific pharmacological model for drugs effective against generalized tonic/clonic and focal cortical epilepsies in humans. 16 references. (Author abstract)

002371 Davis, Kenneth L.; Hollister, Leo E.; Fritz, William C. Veterans Administration Hospital, 3801 Miranda Avenue, Palo Alto, CA 94304 **Induction of dopaminergic mesolimbic receptor supersensitivity by haloperidol.** Life Sciences (Oxford). 23(15):1543-1548, 1978.

To determine if neuroleptics modify the sensitivity of mesolimbic dopaminergic receptors, haloperidol or saline was administered to male Sprague-Dawley rats for 4 weeks. Beginning 8 days after the discontinuation of haloperidol or saline, dopamine (1.0, 2.5, 5.0, or 10mcg) was injected bilaterally into the nucleus accumbens. Dopamine induced significantly more locomotor activity in rats previously exposed to haloperidol than in saline control animals. Results indicate that haloperidol can produce a supersensitive mesolimbic dopamine receptor in the rat. The implications of these animal findings for human tardive dyskinesia and schizophrenia are discussed. 40 references. (Author abstract modified)

002372 Davis, Stephen F.; Cronin, Elaine L.; Meriwether, Jerry A.; Neideffer, Jerry; Travis-Neideffer, Mary Nell. Austin Peay State University, Clarksville, TN 37040 **Shock-elicited attack and biting as a function of chronic vs. acute insulin injection.** Bulletin of the Psychonomic Society. 12(2):149-151, 1978.

In a paper, which was partially presented at the 1978 annual meeting of the Southern Society for Philosophy and Psychology, the effects of chronic and acute insulin-induced hypoglycemia on attack and biting behavior elicited by tailshock in rats are discussed. Chronic injection subjects had blood sugar level experimentally reduced by insulin for 29 days, including the day of shock testing. Acute injection subjects received an insulin injection only on the day of testing. High levels of attack and biting behavior were shown in the single animal shock elicited aggression situation by the chronic subjects only in experiment 2. The lack of such responding in experiment 1 was attributed to the different injection procedures used in the two experiments. The data are supportive of the proposed negative relationship between hypoglycemia and aggressive responding. 6 references. (Author abstract modified)

002373 Davis, W. Marvin; Smith, Stanley G.; Werner, Toreen E. Department of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **Noradrenergic role in the self-administration of ethanol.** Pharmacology Biochemistry and Behavior. 9(3):369-374, 1978.

Involvement of noradrenergic and/or dopaminergic processes of the brain in self-stimulation behavior toward ethanol was assessed in rats allowed to lever press for 25mg/kg intragastric doses on a CRF schedule. Prior to a reacquisition session, Ss were treated with either saline, alpha-methyl-p-tyrosine (AMT), 1-phenyl-3-(2-thiazolyl)-2-thiourea (U-14,624), or haloperidol. Only the saline pretreated control group and the haloperidol treated Ss reacquired lever press behavior. Groups treated in like fashion, but pressing for a sweet milk reinforcer, all showed reacquisition. Thus, the effects of AMT and U-14,624 are attributed to an interference with the reinforcing effect of ethanol infusions. Brain levels of norepinephrine were by both compounds; dopamine was depleted only by AMT, and serotonin was elevated by 600mg/kg of U-14,624 but unaffected by 300mg/kg. These results suggest that a cerebral noradrenergic system plays an important role in the reinforcing effect of ethanol without an involvement of dopaminergic systems. 32 references. (Author abstract modified)

002374 De Souza, H.; Neto, J. Palermo. Laboratory of Therapeutics, Faculty of Veterinary Medicine, University of Sao Paulo, Sao Paulo, Brazil **Effects of anti-acetylcholine drugs on aggressive behaviour induced by cannabis sativa in REM sleep-deprived rats.** Journal of Pharmacy and Pharmacology (London). 30(9):591-592, 1978.

The effects of pretreament with anti-acetylcholine drugs on aggressive behavior induced by cannabis sativa extracts in REM sleep deprived rats were investigated. Pretreatment intraperitoneal injections of atropine sulphate, scopolamine hydrobromide, and atropine methyl nitrate yielded greatly reduced aggression, reduced aggression, and no reduction in aggression, respectively. The effects are hypothesized to stem from either an unbalance between cholinergic/dopaminergic systems within the brain or a nonspecific blockade of central dopamine receptors at the high doses used. 14 references.

002375 DeBold, Joseph F.; Morris, Julie L.; Clemens, Lynwood G. Department of Psychology, Carnegie-Mellon University, Pittsburgh, PA 15213 **The inhibitory actions of progesterone: effects on male and female sexual behavior of the hamster.** Hormones and Behavior. 11(1):28-41, 1978.

The inhibitory effects of progesterone on estrogen-induced and androgen-induced sexual behaviors were compared in male and female hamsters. In Experiment 1, chronic progesterone treatment was found to have no effect on male copulatory behavior maintained after castration with testosterone propionate or estradiol benzoate. However, testosterone propionate was more effective at maintaining male behavior than was estradiol benzoate. In the second experiment, progesterone was found to have a slight inhibitory effect on the rate of restoration of the intromission response after androgen treatment in males which had been castrated for 8 weeks. In the final experiment, chronic progesterone treatment markedly inhibited sexual receptivity in male and female hamsters which had been given 4 weeks of androgen or estrogen treatment and a single pretest injection of progesterone. Thus, progesterone was shown to be a potent inhibitor of androgen-induced and estrogen-induced estrus in both male and female hamsters. Due to the large difference in effectiveness on these two behavioral systems, it is suggested that progesterone affects steroid-induced male copulatory behavior and female receptivity by different mechanisms of action. 56 references. (Author abstract modified)

002376 Deviche, Pierre. Laboratoire de Biochimie Generale et Comparee, 17, Place Delcour, B-4020 Liege, Belgium **Effects of testosterone propionate and pituitary-adrenal hormones on the social behaviour of male ducklings (Anas platyrhynchos L.) in two test situations.** Zeitschrift fur Tierpsychologie (Berlin). 49(1):77-86, 1978.

The behavioral influence of testosterone propionate (TP) injections, combined with pituitary-adrenal hormone administration, was studied in male ducklings in two test situations: in groups of birds from the same residence cage or from visually isolated cages. TP administration seemed to increase sexual but not aggressive behavior, while pituitary-adrenal hormones induced very few effects. The responses of the birds were modulated to a large extent by the type of test situation. 32 references. (Journal abstract modified)

002377 Diakow, Carol; Wilcox, Josiah N.; Woltmann, Richard. Biology Dept., Adelphi University, Garden City, NY 11530 **Female frog reproductive behavior elicited in the absence of the ovaries.** Hormones and Behavior. 11(2):183-189, 1978.

Female frog reproductive behavior elicited in the absence of the ovaries was investigated. A release croak is emitted by unreceptive female frogs when they are clasped around the trunk;

receptive females are silent. In one experiment, ovariectomized females given extradiol and/or progesterone continued to croak at a rate equivalent to that of unreceptive females. In another experiment, the frequency of emission of the croak was reduced significantly by artificial distension of ovariectomized females with fluid. These experiments fail to show a role for ovarian steroids in the reproductive behavior of the female frog, and demonstrate that breeding behavior can be induced in female frogs in the absence of ovarian hormones. These results are consistent with the interpretation that the release croak is inhibited by a mechanism that involves water uptake. 18 references. (Author abstract modified)

002378 Dohan, F. C.; Levitt, D. R.; Kushnir, L. D. Eastern Pennsylvania Psychiatric Institute, Philadelphia, PA **Abnormal behavior after intracerebral injection of polypeptides from wheat gliadin: possible relevance to schizophrenia.** Pavlovian Journal of Biological Science. 13(2):73-82, 1978.

The question of whether or not relatively small quantities of glutamine-glutamic acid proline rich polypeptides from dietary gliadin (from wheat gluten), when injected into the brain would produce abnormal behavior was studied. To test these drug effects on the behavior of normal rats, the protective barrier systems were bypassed by intracerebral injection of a potent subfraction of gliadin polypeptides which produces psychiatric symptoms in celiac patients. Eighteen exploratory experiments in four rats demonstrated that intracerebral injection of these polypeptides may variably produce stereotyped movements, prolonged ""chewing in air," catalepsy and seizures, all after an unusually long latent period. The lowest dose producing catalepsy was 600microg, and that for seizures was 500microg. Since a mixture was used, one or more polypeptides in it may be considerably more potent. The accumulated evidence suggests the following working hypothesis: one or more of the polypeptides produced by peptic pancreatic digestion of certain glutamine proline rich food proteins (e.g.,cereal grain glutens) are psychotoxic and may enter the brain of the schizophrenic or celiac because the small gut, and possibly other barrier systems (enzymatic, immunologic, membranous,) suffer defects of an unknown nature due to one or more abnormal genes common to both diseases; and that the differences in the two diseases are determined largely by the dissimilar components of the genotypes. 19 references. (Author abstract modified)

002379 Dourish, C. T.; Cooper, S. J. Dept. of Psychology, Queen's University of Belfast, Belfast, Northern Ireland **Effects of ET 495 (Piribedil) on water intake in the rat: evidence for a dopaminergic involvement in thirst.** Irish Journal of Medical Science (Dublin). 147(Supplement 1):19-23, 1978.

A paper read at the first Irish Psychopharmacology Conference, held in Belfast in March 1978, is presented. The effects of ET495, Piribedil, on rat water intake was examined. ET 495 is a central dopamine receptor agonist with long-lasting behavioral and biochemical effects. ET 495 is converted into an active catechol metabolite, S-584, and this appears to be responsible for the central effects of the parent compound. ET 495 can exacerbate symptoms in schizophrenics, but has some therapeutic efficacy in patients with Parkinson's disease. Both actions can be related to its status as a central dopamine agonist. The proposal that dopaminergic pathways may be involved in the control of drinking behavior was explored. ET 495 was found to attenuate drinking induced by either injection of hypertonic NaCl or water deprivation. 27 references. (Author abstract modified)

002380 Downs, David A.; Harrigan, Stephen E.; Wiley, James N.; Robinson, Thomas E.; Labay, Robert J. Dept. of Pharmacology, Warner-Lambert/Parke-Davis Pharmaceutical Research Division, 2800 Plymouth Road, Ann Arbor, MI 48105 **Continuous stimulant self-administration in rhesus monkeys.** Research Communications in Psychology, Psychiatry and Behavior. 4(1):39-49, 1979.

The effects of self-administration of high doses of stimulants in rhesus monkeys were investigated. In groups of three or four monkeys with 30 days drug self-administration experience, cocaine, d-amphetamine, and methylphenidate self-administration resulted in weight loss, stereotypy, and at least one death per group. Continuous d-amphetamine availability did not cause deaths in a group of three monkeys with no previous self-administration experience. With all drugs, erratic cycles of increasing and decreasing intake occurred across days of exposure. It is suggested that the lower incidence of toxic effects of cocaine and d-amphetamine than in previous reports may be related to the small number of subjects in such experiments or to other unspecified factors. It is concluded that lethal levels of drug intake are not inevitable consequences of stimulant self-administration. 5 references. (Author abstract modified)

002381 Dudek, Bruce Craig. State University of New York at Binghamton **Dopaminergic involvement in the genetic modulation of neurosensitivity to ethanol. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 7818066, HC$15. MF$7.50. 169 p. 1978.

A series of studies were undertaken to examine dopaminergic involvement in the genetic modulation of neurosensitivity to ethanol in mice bred for sensitivity (LS) or insensitivity (SS) to alcohol. Studies included: ethanol effects in conditioned taste aversion; ethanol affects on locomotor performance in a passive-avoidance task; pharmacological analysis of response to gamma-butyro-lactone (GBL) in a variety of motor coordination and activity tests; amphetamine effects on GBL-induced depression of activity; and amphetamine effects on ethanol responsivity. Findings provide support for catecholamine involvement in the expression of genetic differences in ethanol neurosensitivity. The increase in dopamine synthesis following GBL treatment was greater in LS than SS mice, indicating a marked difference in the dopamine systems of the two strains. This model of LS and SS physiology is thought to extend to differences in motor response to ethanol across a variety of genotypes. (Journal abstract modified)

002382 Elchisak, M. A.; Rosecrans, J. A. Section on Experimental Therapeutics, Laboratory of Clinical Science, NIMH, NIH, Bethesda, MD 20014 **Development of morphine tolerance and physical dependence in rats depleted of brain catecholamines by 6-hydroxydopamine.** Neuropharmacology (Oxford). 18(2):175-182, 1979.

In a study of the role of brain catecholamines in the development of morphine tolerance and physical dependence, Sprague-Dawley rats were permanently depleted of brain norepinephrine (NE) and dopamine (DA) by 6-hydroxydopamine (6-OHDA) or preferentially depleted of brain DA by 6-OHDA plus desmethylimipramine at 2 weeks of age. Beginning 5 weeks later, morphine was injected twice daily for 32 days. A decreased antinociceptive response to morphine was seen in DA depleted rats in both the nontolerant and tolerant states, but the development of tolerance was not affected. The antinociceptive affect of morphine was not modified in tolerant or nontolerant rats depleted of both NE and DA, and the development of tolerance was not affected in these rats. The spontaneous withdrawal syndrome after abrupt cessation of morphine after 32 days treatment was markedly enhanced in rats depleted of NE and DA. Results suggest that DA may be involved in mediating the antinociceptive effect of morphine, but not in the development of tolerance to that affect. 28 references. (Author abstract modified)

002383 Ettinger, Richard H.; Thompson, Richard W. Department of Psychology, Washington State University, Pullman, WA 99164 **The role of dopaminergic systems in the mediation of tonic immobility (animal hypnosis) in chickens.** Bulletin of the Psychonomic Society. 12(4):301-302, 1978.

To further investigate the role of dopaminergic systems (catecholamines) in the mediation of tonic immobility (TI) in chickens, three groups of 10 cockeral chicks were injected with distilled water or with 50 or 100mg/kg of L-DOPA (L-3,4-dihydroxyphenylalanine) before testing for TI duration. Results indicate that chicks injected with 100mg/kg of L-DOPA had longer durations of TI than those injected with distilled water. These results suggest a mediating role of dopaminergic pathways in TI. 12 references. (Author abstract)

002384 Evans, Hugh L.; Weiss, Bernard. Institute of Environmental Medicine, New York University Medical Center, New York, NY 10016 **Behavioral toxicology.** In: Blackman, D., Contemporary research in behavioral pharmacology. New York, Plenum, 1978. 506 p. (p. 449-487).

The behavioral effects of environmental chemicals are explored. Topics discussed include: origins of behavioral toxicology; similarities between pharmacology and toxicology; qualitative evaluation of effects; the role of threshold estimates; the chronicity factor; complications associated with chronic studies; multidisciplinary features; behavioral toxicology in the Soviet Union; mercury; lead; carbon monoxide; pesticides; volatile anesthetics and solvents; modulating factors such as diurnal rhythms, degree of schedule control, discriminative stimuli, and stimulus complexity; food additives; behavioral teratology; evaluations in the natural enviroment; and premarket screening of all new chemicals. 142 references.

002385 File, Sandra E. Dept. of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Anxiety, ACTH, and 5-HT.** Trends in Neurosciences (Amsterdam). 1(1):9-11, 1978.

An animal model of anxiety for use in testing the mode of action of current anxiolytic drugs, mainly the benzodiazepines, is described. Level of social interaction in rats was demonstrated to be inversely related to level of anxiety. The anxiogenic effects of corticotrophin (ACTH) were studied through the rat anxiety model. The hypothesis that important sites of action of ACTH are serotonin pathways is discussed, along with the clues that the hypothesis gives to the possible mechanism of action of anxiolytic drugs such as Librium. 5 references.

002386 File, Sandra E. Department of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **ACTH, but not corticosterone impairs habituation and reduces exploration.** Pharmacology Biochemistry and Behavior. 9(2):161-166, 1978.

Administration of the adrenocorticotrophic hormone fragment ACTH1-24 impaired the habituation of an orienting response to auditory stimuli in male hooded rats (Rattus norvegicus). Corticosterone had no effect on habituation, whereas ACTH4-10, which does not release corticosterone, impaired habituation. Both ACTH1-24 and ACTH4-10 reduced the level of exploration measured in a holeboard, but corticosterone had no significant effect. ACTH did not impair habituation of exploration, suggesting that different mechanisms are responsible for habituation of orienting and habituation of exploration. Results are consistent with the hypothesis that ACTH is anxiogenic. 35 references. (Author abstract modified)

002387 File, Sandra E.; Vellucci, Sandra V. Department of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Studies on the role of ACTH and of 5-HT in anxiety, using an animal model.** Journal of Pharmacy and Pharmacology (London). 30(2):105-110, 1978.

The involvement of adrenocorticotropic hormone (ACTH) and of the serotonin (5-hydroxytryptamine, 5-HT) system in the production of anxiety were evaluated using a new animal model of anxiety in which the time spent by pairs of male rats in active social interaction is measured under various test conditions. ACTH had an anxiogenic effect that was maximal during a 10 min test period starting 3 min after injection. The behavioral effects of ACTH were counteracted by chronic administration of chlordiazepoxide for 5 days before the social interaction test and by acute administration of ethanol 30 min prior to the test. These anxiolytic drugs decreased the turnover of 5-HT in the midbrain and hypothalamus. It is proposed that anxiety results from the action of ACTH, possibly on 5-HT pathways in the midbrain and hypothalamus. 23 references. (Author abstract modified)

002388 Fletcher, T. J. Reedie Hill Farm, Auchtermuchty, Fife, Scotland **The induction of male sexual behavior in red deer (Cervus elaphus) by the administration of testosterone to hinds and estradiol-17beta to stags.** Hormones and Behavior. 11(1):74-88, 1978.

The behavioral effects of androgens and estrogens were studied in free living and enclosed male red deer (Cervus elaphus). One gram implants of testosterone were placed subcutaneously in two adult intact and one castrated red deer hinds, and 100mg implants of estradiol-17beta were given to three castrated and two intact red deer stags. Sexual behavior was observed in the wild and in captivity for 3 years. Testosterone initially produced prolonged and intense estrous behavior in the hinds, and this was followed by rutting behavior. Testosterone implanted hinds rose in the dominance hierarchy as measured by competition for food. Pregnancy, or the administration of progestagens, suppressed most of this behavior. Estradiol-17beta mimicked the behavioral effects of testosterone when given to castrated stags, stimulating all components of rutting behavior. In intact stags, the only effects were to abolish antler casting and stimulate roaring; normal rutting behavior continued unchanged. In contrast to the effects of testosterone, estradiol-17beta did not influence the social status of castrated or intact stags. 13 references. (Author abstract modified)

002389 Fujiwara, Michihiro; Ueki, Showa. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu University 62, Fukuoka 812, Japan **The course of aggressive behavior induced by a single injection of delta9-tetrahydrocannabinol and its characteristics.** Physiology & Behavior. 22(3):535-539, 1979.

The effect of delta9-tetrahydrocannabinol (THC) on muricide and rod attack behavior was investigated in virgin female Wistar King A rats. In animals housed in isolation for 1 day, during which food was available for only 2 hours, a single dose of THC resulted in marked muricide and rod attack behavior; this continued for 100 days after THC treatment in rats maintained in isolation. These animals also showed rat pup killing behavior. When animals were transferred to group housing 60 days after THC treatment, rod attack behavior disappeared completely and muricide disappeared in 13 of 28 rats. However, when these rats were returned to isolation after a 15 day period of group housing, rod attack behavior and muricide reappeared. It is concluded that housing condition plays a crucial role in the occurrence and maintenance of THC-induced aggression. 26 references. (Author abstract modified)

002390 Giedt, W. R., Jr.; Lakin, M. L.; Winters, W. D. Department of Pharmacology, University of California, Davis, CA 95616 **Diurnal response to ketamine and gamma-hydroxybutyrate and its possible relationship to pineal indoleamines.** Neuropharmacology (Oxford). 17(4/5):221-228, 1978.

A diurnal cycle of ketamine and gamma-hydroxybutyrate (GHB) induced catatonia was demonstrated in chicks. The response to ketamine and GHB was lowest at mid light and highest at mid dark. Pinealectomy abolished the dark induced increase in response to both agents. Sham pinealectomized chicks responded in the same manner as did intact chicks. When chicks were pretreated with serotonin, N-acetylserotonin, or melatonin, the ketamine response was augmented; melatonin was the most potent of the indoleamines tested in augmenting the ketamine response. The pineal gland, associated with the dark period of the day, appears to influence response to both ketamine and GHB in the chick. 31 references. (Author abstract)

002391 Glennon, Richard A.; Rosecrans, John A.; Young, Richard; Gaines, Judith. Dept. of Pharmaceutical Chemistry, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Hallucinogens as a discriminative stimuli: generalization of DOM to a 5-methoxy-N,N-dimethyltryptamine stimulus.** Life Sciences (Oxford). 24(11):993-997, 1979.

The tryptamine analogue 5-methoxy-N,N-dimethyltryptamine (5-OME DMT) served as a discriminative stimulus in male Sprague-Dawley rats trained to respond under a variable interval 15 second schedule of food reinforcement. The 5-OMe DMT stimulus was attenuated by the serotonin antagonist BC-105. The 5-OMe DMT stimulus generalized with 2,5-dimethyl-4-methylamphetamine (DOM), suggesting that 5-OMe DMT and DOM produce qualitatively similar interoceptive cues in rats. 14 references. (Author abstract modified)

002392 Glick, Stanley D.; Cox, Russell D. Dept. of Pharmacology, Mount Sinai School of Medicine, City University of New York, New York, NY 10029 **Nocturnal rotation in normal rats: correlation with amphetamine-induced rotation and effects of nigrostriatal lesions.** Brain Research (Amsterdam). 150(1):149-161, 1978.

The effects of nigrostriatal lesions on nocturnal rotation in naive female Sprague-Dawley rats and on D-amphetamine-induced day time rotation were investigated. Normal unoperated rats were observed to rotate (turn in circles) at night. For most (91.7%) rats, the preferred direction of rotation was consistent across hours and days and was the same as the direction of rotation elicited by d-amphetamine (1.0mg/kg) during the day. The magnitudes of nocturnal and d-amphetamine-induced rotation were also highly correlated. After rats showed stable diurnal pattens of rotation, unilateral lesions were made in either the substantia nigra, the nigrostriatal bundle or the caudate nucleus. All lesions produced transient contralateral rotation within the first 24-48 hours after surgery. The time course of this contralateral rotation was more prolonged after nigral lesions than after nigrostriatal bundle lesions and least after caudate lesions, suggesting that the duration of a degeneration release of dopamine is proportional to the length of the degenerating axon. Lesion size was correlated with the intensity of contralateral rotation but not with the time course. At each rostral/caudal level, the magnitude of contralateral rotation was greater if the lesion was in the side of the brain opposite to the preoperative direction of rotation than if in the same side. By 3 days after surgery, all rats returned to a mostly normal diurnal cycle with the direction of rotation now being ipsilateral to the lesion. D-amphetamine potentiated the ipsilateral rotation, though rats with lesions in the same side of the brain as the preoperative direction of rotation had larger drug responses than rats with similar lesions in the opposite side of the brain. By 1 month after surgery, the direction of spontaneous rotation of most rats had returned to the preoperative direction. It is suggested that compensatory processes occur to a greater extent if the lesion is in the normally more active side of the brain. 17 references. (Author abstract modified)

002393 Goldfoot, David A.; Wiegand, Stanley J.; Scheffler, Guenther. Wisconsin Regional Primate Research Center, University of Wisconsin, Madison, WI 53706 **Continued copulation in ovariectomized adrenal-suppressed stumptail macaques (Macaca arctoides).** Hormones and Behavior. 11(1):89-99, 1978.

Possible explanations for an earlier finding that female stumptailed macaques continue to copulate at moderate to high levels for years after gonadectomy were examined. The extent to which sexual behavior of ovariectomized females was maintained by steroids of adrenal origin was studied, and the possibility that ovarian fragments might have been left in situ following surgery was considered. Within the limits to which sex steroids were suppressed by daily injections of .1mg of dexamethosone sodium phosphate, no correlations were found between steroid levels and sexual performance. Ejaculatory frequencies and measures of attractivity, proceptivity, and receptivity collected during heterosexual pair tests remained unaffect in all four females during 4 weeks of dexamethasone treatment. Thus it was concluded that the maintenance of copulatory activity after ovariectomy in this species is largely due to nonsteroidal mechanisms. 20 references. (Author abstract modified)

002394 Gorelick, David A.; Catlin, Don H.; George, Robert; Li, Choh Hao. Department of Psychiatry, University of California, Los Angeles, CA 90024 **Beta-endorphin is behaviorally active in rats after chronic intravenous administration.** Pharmacology Biochemistry and Behavior. 9(3):385-386, 1978.

Behavioral activity was investigated in male Sprague-Dawley rats after 14 daily intravenous injections of saline or human beta-endorphin (2.5mg/kg). Animals were given one way active avoidance training on the eleventh day and analgesia testing on the twelfth (tail flick) and thirteenth (hot plate) days. Beta-endorphin had no effect on the number of trials needed to reach the avoidance criterion, but significantly lengthened response latencies as compared with saline injections. Beta-endorphin had no analgesic effect in either test procedure. 12 references. (Author abstract modified)

002395 Greer, C. A.; Alpern, H. P. Dept. of Psychology, University of Colorado, Boulder, CO 80309 **Differential neurohumoral modulation of myoclonic and clonic seizures.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 236(1):74-85, 1978.

Differential effects of neuropharmacological drugs upon susceptibility to fluorothyl-induced myoclonic and clonic convulsions were assessed in two selectively bred lines of mice. Dopaminergic drugs only affected myoclonus, whereas cholinergic, GABAergic, and serotonergic compounds principally influenced clonus. Noradrenergic drugs altered the expression of both types of seizures. It is concluded that the results support the idea that myoclonic and clonic convulsions reflect the activity of different physiological processes. 34 references. (Author abstract modified)

002396 Grignolo, A.; Light, K. C.; Obrist, P. A. University of North Carolina, Chapel Hill, NC 27514 **Beta-adrenergic influences on the canine myocardium: a behavioral and pharmacological study.** Psychophysiology. 15(3):288-289, 1978.

A summary is presented of a report on the cardiovascular responses of the dog to the onset of a behavioral stressor, and on

the activation of cardiac beta-adrenergic receptors as assessed with the use of the relatively cardiospecific beta-blocker practolol (PCT), which was delivered to the Seventeenth Annual Meeting of the Society for Psychophysiological Research, held in Philadelphia, October 1977. Pharmacological inotropic manipulations were included in the experiment. With regard to stress onset, the acute responses lasted approximately 40 sec and included elevations of systolic blood pressure (BP), heartrate (HR), dP/dt, dLVP/dt, stroke volume, and cardiac output which were significantly reduced by PCT. A small elevation of diastolic BP was unaffected by beta-blockade. The results indicate that both dP/dt and dLVP/dt are sensitive to beta-adrenergic influences on the heart and less susceptible than HR to the effects of vagal withdrawal; dLVP/dt has higher gain than dP/dt. It is concluded also that the cardiac response to stress onset includes a significant beta-adrenergic component which mediates phasic elevations of systolic blood pressure. (Author abstract modified).

002397 Gronan, Robert J.; York, Donald H. Department of Physiology, West Virginia School of Osteopathic Medicine, Lewisburg, WV 24901 **Effects of chronic intraventricular administration of angiotensin II on drinking behavior and blood pressure.** Pharmacology Biochemistry and Behavior. 10(1):121-126, 1979.

The effects of continuous infusion of angiotensin II (AII) into lateral cerebral ventricle on daily food and water consumption, urine volume, and aortic blood pressure were studied in male Sprague-Dawley rats. AII was infused at a rate of 10ng/hour for 7 days, using subcutaneously implanted osmotic minipumps; an intraventricular (IVT) control group was infused only with the saline vehicle, and a third group received subcutaneous AII. The IVT AII rats showed a four fold increase in water consumption, to a mean of 171ml/day during days 2 through 4 of infusion; water intake did not change in the other groups. Urine volume showed a similar pattern, increasing five fold in the IVT AII group during days 2 through 4. These measures declined during the final 3 days of AII infusion, but significant tolerance was not observed. Food intake decreased markedly in both saline and IVT AII groups after implantation of the pumps, but the latter resumed normal food intake more slowly than the saline group. Body weight remained below preinfusion levels throughout the AII period. Aortic blood pressure of the IVT AII rats showed a slight rise during the infusion period, but did not significantly exceed that of saline controls. 22 references. (Author abstract modified)

002398 Guest, James; Consroe, Paul. Department of Pharmacology and Toxicology, University of Arizona College of Pharmacy, Tucson, AZ 85721 **Psilocybin neuropsychopharmacology in rabbits.** Research Communications in Psychology, Psychiatry and Behavior. 4(1):93-96, 1979.

Quantitative EEG and behavioral effects of intravenous psilocybin and saline were studied in rabbits using a cross-over design with 72 hours between treatments. Psilocybin produced decreases in cortical EEG voltage output, theta and alpha frequencies, and increases in delta and beta energies, concomitant with biphasic alterations in standing and decrements in grooming, rearing, and locomotion behavior. The available data of laboratory animal/human correlations suggest that this rabbit paradigm is suitable for study of psilocybin neuropsychopharmacology. 9 references. (Author abstract)

002399 Haigler, Henry J.; Spring, Denise D. Department of Pharmacology, Emory University School of Medicine, Atlanta, GA 30322 **A comparison of the analgesic and behavioral effects of (D-Ala 2) met-enkephalinamide and morphine in the mesencephalic reticular formation of rats.** Life Sciences (Oxford). 23(12):1229-1239, 1978.

The analgesic effect of (D-Ala 2) met-enkephalinamide (DALA) injected intracerebrally (IC) upon the mesencephalic reticular formation (MRF) of unanesthetized rats was studied; and the analgesia produced by DALA and morphine was compared. DALA injected intracerebrally at low doses into specific sites of the MRF produced a profound, long lasting analgesia that was blocked by naloxone, a specific opiate antagonist. Morphine was only half as potent as DALA because morphine, injected IC at similar sites in the MRF, yielded a comparable analgesia only when injected at twice the dose. The analgesic effects of morphine were also antagonized by naloxone. Both DALA and morphine produced specific behavioral effects. Naloxone blocked the behavioral effects of DALA, but not those produced by morphine. 19 references. (Author abstract modified)

002400 Handley, S. L.; Thomas, K. V. Dept. of Pharmacy, Gosta Green, Birmingham B4 7ET, England **On the mechanism of amphetamine-induced behavioural changes in the mouse. II. Effects of agents stimulating noradrenergic receptors.** Arzneimittel Forschung (Aulendorf). 28(5):834-837, 1978.

The effects of three noradrenergic stimulants, norepinephrine and alpha-methylnorepine phrine administered into the cerebral ventricles and of parenterally injected clonidine, were observed in 18 items of dexamphetamine-induced behavior in the mouse. Stereotyped behavior was depressed by the noradrenergic stimulants except for compulsive gnawing, which was markedly enhanced. Aspects of locomotor activity were enhanced excedpt when compulsive gnawing was strong, at which time they were suppressed. Elements of heightened arousal were enhanced. It is suggested that these may be a positive noradrenergic component in the genesis of compulsive gnawing, locomotor activity, and heightened arousal. The dominance of compulsive gnawing over certain other dexamphetamine-induced behaviors may indirectly lead to the suppressor effects of the noradrenergic stimulants on these behaviors. 29 references. (Author abstract)

002401 Harkins, Jane Schiebel. University of Colorado, Boulder **Biosynthesis of substance-P in cultured mouse neuroblastoma cells and behavioral effects of substance-P in mice. (Ph.D. dissertation).** Dissertation Abstracts International. 39(5):2561-B, 1978. Ann Arbor, Univ. Microfilms No. 7820516, 72p., 1978.

Biosynthesis of substance-P (NH2-Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met-CONH2) in cultured mouse neuroblastoma cells, and behavioral effects of Substance-P in mice were studied. A radioimmunoassay for Substance-P was developed to test for Substance-P in cultured cells. Results show that the antibodies do not cross-react with leu-enkephalin or met-enkephalin, eledoisin or morphine. Very weak binding is observed with met-enkephalinamide. Antibody specificity is determined using Substance-P and its C-terminal or N-terminal fragments. Radioimmunoassays of cultured cells show that the mouse neuroblastoma C1300 and rat C6 glioma cells synthesize Substance-P. Clones of C1300 cells made Substance-P in amounts ranging from 0.20 to 3.30 nanograms/mg protein. The behavioral effects of Substance-P were also studied in C57BL/6J mice. Unilateral infusions of Substance-P into the brain were used to determine if the peptide would produce morphine-like dependence. Substance-P infusions into the substantia nigra result in a state where naloxone induces rearing behavior very similar to morphine, but no jumping behavior. Contralateral rotational behavior is also observed in the mice with nigral morphine fusions 1 to 4 hours after minipump implantation. Infusions of Substance-P to the substance nigra produce contralateral turning in half of the mice tested. This rotational behavior developed after several

days and was not blocked by naloxone. (Journal abstract modified)

002402 Heal, D. J.; Phillips, A. G.; Green, A. R. MRC Unit, University Department of Clinical Pharmacology, Radcliffe Infirmary, Oxford OX2 6HE, England **Studies on the locomotor activity produced by injection of dibutyryl cyclic 3'5'AMP into the nucleus accumbens of rats.** Neuropharmacology (Oxford). 17(4/5):265-270, 1978.

Bilateral injection of dibutyryl cyclic adenosine monophosphate (AMP, 5-25mcg) into the nucleus accumbens of male Sprague-Dawley rats produced an increase in coordinated locomotor activity lasting about 90 minutes, as well as behavioral changes similar to those produced by dopamine (DA). Pretreatment with intraaccumbens haloperidol (2.5mcg) had no effect on the locomotor response induced by dibutyryl cyclic AMP (8mcg), but totally abolished the locomotor response to DA (5mcg) in rats pretreated with tranylcypromine (10mg/kg, ip). Haloperidol (0.05mg/kg, ip) inhibited the locomotor response produced by dibutyryl cyclic AMP (12.5mcg) injected into the nucleus accumbens 15 minutes later. Pretreatment with alpha-methyl-p-tyrosine (200mg/kg, ip) 3 hours before dibutyryl cyclic AMP also inhibited the locomotor response. These results suggest the existence of a dopaminergic system postsynaptic to the nucleus accumbens. Aminooxyacetic acid (25mg/kg) produced an inhibition of the dibutyryl cyclic AMP locomotor activity 90 minutes later, suggesting a possible inhibitory influence of GABA on brain dopaminergic systems. 26 references. (Author abstract modified)

002403 Heller, Knud Erik. Zoological Laboratory, University of Copenhagen, Universitetsparken 15, DK-2100 Copenhagen, Denmark **Role of corticosterone in the control of post-shock fighting behaviour in male laboratory mice.** Behavioural Processes (Amsterdam). 3(3):211-222, 1978.

To examine the role of corticosterone in controlling fighting subsequent to electric footshock in 96 male mice, two experiments were conducted. It was found that: 1) treatment with corticosterone restores post shock fighting in adrenalectomized males but not in castrated adrenalectomized males; 2) raising corticosterone levels induces postshock fighting in castrated adrenalectomized males treated with testosterone but not in castrated adrenalectomized controls treated with a placebo; and 3) preventing corticosterone responses to shock occludes the increase in fighting which normally follows shock in intact males. These findings suggest that: 1) corticosterone plays an important role in the control of postshock fighting in mice; 2) the importance of corticosterone is dependent of the presence of circulating testosterone or other androgens; and 3) corticosterone responses to the experience of shock may be involved in the mediation of the facilitating effects of this experience on subsequent fighting behavior. 26 references. (Author abstract modified)

002404 Hine, B.; Sakalis, G.; Gershon, S. Department of Psychiatry, New York University School of Medicine, 550 First Avenue, New York, NY 10016 **Antagonism of amphetamine-induced stereotyped behavior in dogs by thioridazine and mesoridazine.** Research Communications in Psychology, Psychiatry and Behavior. 4(1):89-92, 1979.

The efficacy of thioridazine and mesoridazine in modifying stereotyped behavior was investigated in eight dogs. Behavior was observed continuously for 2 hours after amphetamine injection and stereotypic behavior was rated. The data indicate that mesoridazine pretreament 1.5hours before amphetamine challenge effectively attenuated or blocked stereotyped behavior better than half thioridazine at half the thiroridazine dose. Although the underlying mechanisms are not known, it is suggested that: 1) metabolites are present after thioridazine but not mesoridazine administration that may compromise the neuroleptic effectiveness of thioridazine; 2) thioridazine metabolites other than mesoridazine may be responsbile for this drug's action; or 3) mesoridazine is a more effective receptor blocker than thioridazine. It is suggested that the failure of thioridazine to block amphetamine stereotypy and the relatively moderate attenuation of stereotype at 1.5hours cannot be attributed to a lack of mesoridazine in plasma at this time. Similarly, elevated plasma levels of the ring sulfoxide of thioridazine were also present in the kinetic study. Elevated sulfoxide levels were observed up to 20 hours after thioridazine administration. Further investigation of metabolite hypotheses of neuroleptic action is recommended. 6 references.

002405 Holaday, John W.; Dallman, Mary F.; Loh, Horace H. Dept. of Medical Neurosciences, Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington, DC 20012 **Effects of hypophysectomy and ACTH on opiate tolerance and physical dependence.** Life Sciences (Oxford). 24(9):771-781, 1979.

In opiate naive, hypophysectomized male Long-Evans rats, the enhanced potency of parenterally injected morphine was almost completely normalized by chronic adrenocorticotropic hormone (ACTH) in doses that maintained adrenal weight. Following morphine pellet implantation, the amount of morphine required for antinociception, catalepsy, and colonic temperature effects in tolerant rats was identical in hypophysectomized and sham operated rats, whether or not chronic ACTH was administered. However, brain levels of morphine were greater in tolerant, hypophysectomized rats, and this effect was blocked by chronic ACTH. In general, hypophysectomy and/or ACTH did not modify the intensity of abstinence signs following naloxone precipitated withdrawal. Results suggest a secondary adrenal involvement rather than direct pituitary mediation of chronic opiate effects. 32 references. (Author abstract modified)

002406 Holtzman, Stephen G. Department of Pharmacology, Emory University School of Medicine, Atlanta, GA 30322 **Suppression of appetitive behavior in the rat by naloxone: lack of effect of prior morphine dependence.** Life Sciences (Oxford). 24(3):219-226, 1979.

Naloxone (0.3-10mg/kg) produced a dose related suppression of eating and drinking in male Sprague-Dawley rats that had been deprived of food for 48 hours or deprived of water for 24 hours. The suppression of water intake by naloxone was unaltered in rats that had been physically dependent on morphine 1 week earlier and tolerant to the effect of morphine at the time naloxone was tested. These results indicate that naloxone can suppress appetitive behavior in the rat, but do not resolve the issue of whether this naloxone effect is the result of an interaction with an edogenous opioid system. 36 references. (Author abstract)

002407 Horita, A.; Carino, M. A. Dept. of Pharmacology, School of Medicine, University of Washington, Seattle, WA 98195 **Analeptic and antianaleptic effects of naloxone and naltrexone in rabbits.** Life Sciences (Oxford). 23(16):1681-1686, 1978.

Naloxone (5mg/kg), but not naltrexone, shortened the duration of anesthesia in male New Zealand rabbits pretreated with pentobarbital. This analeptic effect was blocked by atropine, but not by methylatropine, indicating the involvement of a central cholinergic mechanism. Smaller doses of both naloxone antagonized the analeptic property of d-amphetamine. In conscious animals, naloxone potentiated and naltrexone attenuated the excitatory effects of TRH and d-amphetamine. 11 references. (Author abstract modified)

002408 Horowitz, Gary Paul. Florida State University **Genetic influences on preference for and effects of morphine in mice. (Ph.D. dissertation.)** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 7801484, HC$15. MF$7.50. 126 p. 1977.

Three experiments are presented in which the role of genetic factors and the vehicle of the drug in determining the amount of morphine that mice consume under various oral ingestion procedures were investigated. In one experiment, mice of two inbred strains (C57 and DBA) and their derived reciprocal F1 hybrids (CD and DC) were offered daily choices between water and morphine, saccharine, or a saccharin/morphine mixture. In a second experiment, male and female DBA mice were offered various concentrations of morphine sulfate in a saccharine vehicle and water in a free choice test situation. In the third experiment, C57 and DBA mice and their reciprocal F1 hybrids were exposed to 10 days of forced morphine ingestion, and then withdrawn by replacing the morphine solution with water. The results of the three experiments suggest a relationship among mice between the predisposition to ingest morphine adulterated solutions (behavioral dependence liability) and the effects of morphine on activity. It was found that this relationship is mediated, in part, genetically. (Journal abstract modified)

002409 Hraschek, A.; Endroczi, E. Central Research Division, Postgraduate Medical School, Budapest, Hungary. **Effects of systemic and intracerebral administration of adrenergic receptor blocking drugs on the conditioned avoidance behavior and maze learning in rats.** Psychoneuroendocrinology (Oxford). 3(3/4):271-277, 1978.

Effects of alpha-adrenergic and beta-adrenergic receptor blocking drugs, given systemically or intracerebrally into the brainstem, were studied on the acquisition, retention, and extinction of conditioned avoidance behavior. The systemic administration of beta-adrenergic receptor blockers, Trasicor and GYKI 41099, led to a marked suppression of the acquisition of a two-way avoidance response, but did not modify the retention or the extinction of the avoidance response. Injection of GYKI 41099 into the brainstem reticular formation resulted in a decrease in the acquisition of the conditioned avoidance response. The same treatment with an alpha-adreneric receptor blocker, phenoxybenzamine, failed to influence the acquisition of the conditioned avoidance response. These observations suggest that beta-adrenergic receptors are involved in modulating the acquisition of a conditioned response, although they do not play a significant role in the retention or the extinction processes. 22 references. (Author abstract modified)

002410 Huang, J. T. Institute of Neurochemistry, Ward's Island, New York, NY 10035 **Morphine effects on mouse jumping behavior induced by high ambient temperature.** Research Communications in Psychology, Psychiatry and Behavior. 4(1):31-38, 1979.

High ambient temperature induced jumping in mice was investigated with opiate narcotics and some central nervous system drugs. Morphine, levorphanol, physostigmine, and tremorine can inhibit jumping induced by 35 to 37 degrees celcius ambient temperature. The dose of morphine required to inhibit jumping is less than the dose to produce analgesia. All other drugs that have been tested do not inhibit jumping. Chlorpromazine increased the jumping behavior. When comparison between naloxone-induced jumping and high-ambient temperature-induced jumping as effected by drugs was made, most drugs produced a similar effect on both types of jumping. These results suggest that naloxone or high ambient temperature activate the same neuroanatomical system to induce jumping. 13 references. (Author abstract)

002411 Hull, Elaine M.; l'Hommedieu, Georgia; Kastaniotis, Chris; Franz, Jonathan R. Department of Psychology, State University of New York at Buffalo, 4230 Ridge Lea Road, Amherst, NY 14226 **Pituitary/adrenal hormones do not influence bulbectomy-induced behavioural changes.** Physiology & Behavior. 22(3):417-421, 1979.

The roles of cortisol and adrenocorticotrophic hormone (ACTH) in the development of irritability and hyperactivity after olfactory bulbectomy were investigated. Dexamethasone phosphate (which suppresses ACTH and, indirectly, cortisol), metyrapone (which inhibits production of cortisol and indirectly increases ACTH), or saline were injected daily in male Mongolian gerbils previously given bilateral olfactory bulbectomies or sham operations. Bulbectomized animals were more active in an open field apparatus, were more aggressive in grouped and paired social interaction tests, and initiated more nonaggressive contacts in paired social interaction tests than sham operated controls. Both dexamethasone and metyrapone led to increased activity in the open field, but did not significantly affect any other measure. Neither dexamethasone nor metyrapone significantly decreased any of the behavioral changes resulting from bulbectomy. Results suggest that physiological levels of the pituitary/adrenal hormones are not essential for bulbectomy-induced behavioral changes in the gerbil. 22 references. (Author abstract modified)

002412 Hwang, Eunyong Chung; Van Woert, Melvin H. Departments of Neurology and Pharmacology, Mount Sinai School of Medicine, Fifth Avenue and 100th Street, New York, NY 10029 **Serotonin-norepinephrine interactions in the tremorolytic actions of phenoxybenzamine and trazodone.** Pharmacology Biochemistry and Behavior. 10(1):27-29, 1979.

Phenoxybenzamine (5mg/kg ip) and trazodone (5mg/kg op) reduced tremors produced in male Swiss-Webster mice by ip administration of oxotremorine (10mg/kg), harmaline (80mg/kg), catechol (60mg/kg), kepone (200mg/kg) and clonidine (100mg/kg). Azapetine (10mg/kg ip) in combination with L-5-hydroxytryptophan (50mg/kg ip) reduced the tremor induced by oxotremorine, catechol, kepone, or clonidine. In mice with lower thoracic spinal cord transection, phenoxybenzamine and trazodone reduced catechol-induced tremor above and below the site of transection. These findings suggest that an alpha-adrenergic/serotonergic neuronal balance in the spinal cord may modulate tremors of different etiologies. 17 references. (Author abstract)

002413 Isaac, W. L.; Isaac, W. University of Georgia, Athens, GA 30602 **Does combining stimulants combine stimulation?** Bulletin of the Psychonomic Society. 12(6):475-476, 1978.

The consequences of combination of moderate doses of amphetamine and methylphenidate, two stimulants commonly used in the treatment of hyperkinesis, on locomotor activity was examined in 12 rats. While a dose related increase in activity was observed for both drugs when administered singly, a combination of the drugs showed only the effect of d-amphetamine. 6 references. (Author abstract modified)

002414 Izumi, Kanji; Butterworth, Roger F.; Tunnicliff, Godfrey; Gonce, Michel; Barbeau, Andre. Department of Neurobiology, Clinical Research Institute of Montreal, 110 Pine Avenue West, Montreal, Quebec, Canada **Possible serotonin-agonist action of veratramine.** Brain Research Bulletin. 3(3):237-240, 1978.

The possible use of serotonin agonists in supressing the excitatory action of veratramine, which produces both tremor and a characteristic struggling behavior, was examined in the rat. This behavioral excitation is accompanied by changes in serotonin content in the hypothalamus. The central serotonin agonist

methysergide in doses of 5-15mg/kg produced a dose dependent inhibition of veratramine's action, while p-chlorophenylalanine had no effect. Results are consistent with a serotonin agonist mechanism to explain veratramine's action. 9 references. (Author abstract)

002415 Jackman, Herbert Lewis. University of Illinois at the Medical Center **5-Hydroxytryptamine and sleeping behavior. (Ph.D. dissertation).** Dissertation Abstracts International. 39(5):2245-B, 1978. Ann Arbor, Univ. Microfilms No. 7818183, 95p., 1978.

The role of 5-hydroxytryptamine (5-HT) in various sleeping behavior mechanisms was studied in four experiments using domestic cats as subjects. The cats were surgically prepared to allow recording of their EEG, electrooculogram, and electromyogram. Sleep parameters studied were: latency to slow-wave sleep (SWS) and paradoxical sleep (PS), and percentage of time spent in wakefulness (W), SWS and PS for total recording time and half hour times. It is concluded that: 1) a properly functioning 5-HT system plays a role in endogenous sleep mechanisms; 2) the endogenous PS mechanism is more sensitive to disruption by 5-HT receptor blockade using methysergide (ME) than is the endogenous SWS mechanism; 3) the SWS mechanism induced by chloral hydrate (CH) or pentobarbitol (PENTO) does not require proper functioning of the 5-HT ME sensitive SWS mechanism found in endogenous sleep; 4) ME pretreatment plus either CH or PENTO treatment shows an additive effect on delaying the appearance of PS; and 5) L-tryptophan pretreatment is capable of partially reversing effects of ME on sleep patterns, but is unable to normalize sleep patterns seen after CH or PENTO. (Journal abstract modified)

002416 Jacobs, Barry L.; Trulson, Michael E. Department of Psychology, Princeton University, Princeton, NJ 08540 **An animal behavior model for studying the actions of LSD and related hallucinogens.** In: Stillman, R., The psychopharmacology of hallucinogens. New York, Pergamon, 1978. 388 p. (p. 220-240).

A paper read at the workshop on assessing hallucinogenic behavior sponsored by the Division of Research of the National Institute on Drug Abuse in Bethesda, Maryland, December 1976, is presented. Lysergic acid diethylamide (LSD) was given to adult female cats and the emergent behaviors of limb flicking, abortive grooming, investigation or playing, and hallucinating were observed. Results are discussed in terms of the dose dependent frequency of behavior, peripheral serotonin blockers, drugs from other classes, other hallucinogens, duration of behavior effects, duration of tolerance, and onset of tolerance. It is proposed that the emergent behaviors in the cat represent a viable animal behavior model for the actions of hallucinogens in humans. The criteria for a valid model are identified. 64 references.

002417 James, T. A.; Starr, M. S. Department of Pharmacology, School of Pharmacy, 29/39 Brunswick Square, London WC1, England **The role of GABA in the substantia nigra.** Nature (London). 275(5677):229-230, 1978.

The effects of decreasing the influence of gamma-aminobutyric acid (GABA) within the substantia nigra with picrotoxin, and of potentiating the action of GABA with cis-1,3 aminocyclohexane carboxylic acid (ACHC, a neuronal GABA uptake inhibitor), on the circling behavior of rats were studied. The direction of turning elicited by intranigral injections of picrotoxin and GABAlike drugs depends on whether these compounds are delivered rostrally or caudally in the substantia nigra. Behavior patterns influenced by the anterior substantia nigra are accompanied by significant changes in homovanillic acid levels in the striatum and require an intact dopamine system. Turning responses initiated by caudal drug injections are apparently not mediated by the dopaminergic nigrostriatal pathway. These findings may explain the contrasting behavioral actions of these drugs which have been reported by different investigators. 14 references.

002418 Kameyama, Tsutomu; Nabeshima, Toshitaka. Department of Chemical Pharmacology, Faculty of Pharmaceutical Sciences, Meijo University, Tenpaku-ku, Nagoya 468, Japan **Effects of 1,3 diphenyl-5-(2 dimethylaminopropionamide)-pyrazole (difenamizole) on a conditioned avoidance response.** Neuropharmacology (Oxford). 17(4/5):249-256, 1978.

The effects of oral analgesic doses of 1,3-diphenyl-5-(2-dimethylaminopropionamide)-pyrazole(difenamizole), morphine, aminopyrine, chlorpromazine, and chlordiazepoxide on the conditioned avoidance response of male Wistar rats were compared. Difenamizole (100-400mg/kg), significantly increased the number of avoidance failures, decreased the number of fecal boluses excreted, and prolonged response latency times. Aminopyrine (100-400mg/kg) produced a dose related prolongation of response latency time, but the effect of aminopyrine on the percentage avoidance was less than that produced by difenamizole at low doses. The avoidance behavior was not significantly influenced by morphine (10-40mg/kg) or chlordiazepoxide (10-40mg/kg). Chlorpromazine (5-20mg/kg) produced a dose related depression in percentage avoidance and a dose related prolongation in response latency time. Results indicate that the effect of difenamizole on conditioned avoidance is similar to that of chlorpromazine. 37 references. (Author abstract modified)

002419 Katz, Richard J. Mental Health Research Institute, Dept. of Psychiatry, University of Michigan Medical Center, Ann Arbor, MI 48109 **ACTH4-10 antagonism of morphine-induced behavioral activation in the mouse.** European Journal of Pharmacology (Amsterdam). 53(4):383-385, 1979.

The 4-10 fragment of adrenocorticotrphic hormone (ACTH4-10) was administered intracerebroventricularly to male C57B1/2J mice, with or without concurrent systemic injection of 50mg/kg morphine sulfate. Morphine produced stereotyped behavioral activation (running, environmental oblivion, and Straub tail), which was antagonized in a dose related fashion by ACTH4-10. Results are consistent with previous findings of opiate/ACTH4-10 interactions in other species and behavioral models. 3 references. (Author abstract modified)

002420 Kelly, Joseph. University of Chicago **GABA: a possible neurochemical substrate for hypothalamic feeding mechanisms. (Ph.D. dissertation).** Dissertation Abstracts International. 39(6):3039-B, 1978. (Not available from Univ. Microfilms), 1978.

In an investigation of the role of GABA in hypothalamic feeding mechanisms, the sensitivity of hypothalamic loci to intracranial injections of the GABA agonist, muscimol and the effect of increased or decreased GABA levels on the anorexia produced by amphetamine or fenfluramine, were studied. Chemical injection and ingestive behavioral studies suggest that both the paraventricular and ventromedial hypothalamic nuclei may be separate though not necessarily independent foci of a GABAergic system. Data from pharmacological analyses and studies of monoamine/GABA interactions suggest that GABA may mediate monoaminergic, but not indolaminergic feeding related systems in the hyptohalamus. (Journal abstract modified)

002421 Kennedy, Brian. Dept. of Pharmacology, University College, Galway, Northern Ireland **Experimental approaches to the detection of anxiolytic activity in the rat.** Irish Journal of Medical Science (Dublin). 147(Supplement 1):38-42, 1978.

A paper read at the first Irish Psychopharmacology Conference, held in Belfast in March 1978, is presented. Four different behavioral tests (the holeboard, fecal counts, food preference, and operant behavior) were assessed for their ability to detect anxiolytic activity in the rat. In evaluating each of these tests, varying doses of anxiolytic compounds were given to the rats and the resulting behavioral changes recorded. Anxiolytics did not significantly alter behavior on the holeboard, nor did they change food preference in accordance with expectations. At high doses anxiolytics reduced fecal counts. While this may be a consequence of the anxiolytic activity of these drugs, their effect on gastric motility per se was not assessed. During the extinction of an operant response anxiolytics consistently shortened the latency before the onset of pressing. It is suggested that this test may be of value in the detection of anxiolytic activity in the rat. 7 references. (Author abstract modified)

002422 Kenny, Marie; Leonard, B. E. Pharmacology Department, University College, Galway, Ireland **Neurochemical and behavioral correlates of chronic apomorphine administration in the rat.** Advances in Biochemical Psychopharmacology. 19:347-349, 1978.

The biochemical effects of chronic treatment with various doses of apomorphine were examined in a series of studies with male Wistar rats. Apomorphine initially induced sniffing and burrowing in most rats, but after 3 days about 30% showed stereotyped fighting, 20% continued to show sniffing/burrowing responses, and 50% exhibited fighting alternated with intense rearing and chewing stereotypy. Sensitivity to apomorphine developed in animals showing the stereotyped fighting response, but not in those showing the sniffing/burrowing response. A second experiment demonstrated a correlation between the chronic dose administered and the nature of the stereotyed response; hypersexuality was associated with lower doses and stereotyped fighting with higher doses. No direct correlation between the nature of the stereotyped response to apomorphine and changes in neurotransmitter concentrations in brain regions functionally implicated in drug-induced stereotypy was observed. 4 references.

002423 Killian, Anthony; Bonese, Kathryn; Rothberg, Richard M.; Wainer, Bruce H.; Schuster, Charles R. Department of Pharmacological and Physiological Sciences, University of Chicago, 947 E. 58th St., Chicago, IL 60637 **Effects of passive immunization against morphine on heroin self-administration.** Pharmacology Biochemistry and Behavior. 9(3):347-352, 1978.

Antimorphine antibodies produced in Rhesus monkeys immunized with morphine-6-hemisuccinate-BSA were passively administered to recipient monkeys trained to self-administer heroin and cocaine. Following antibody administration, changes in heroin self-administration behavior were observed which were similar to those achieved with low doses of naloxone. Both manipulations increased heroin self-administration without affecting cocaine responding. 26 references. (Author abstract)

002424 Klunder, Charles S.; O'Boyle, Michael. University of Southern Mississippi, Hattiesburg, MS 39401 **Suppression of predatory behaviors in laboratory mice following lithium chloride injections or electric shock.** Animal Learning & Behavior. 7(1):13-16, 1979.

The relative effectiveness of electric shock and lithium chloride (LiCL) injections were compared in suppressing cricket killing and eating by mice. Male ICR mice were tested for cricket killing and eating. Mice that attacked and ate a cricket were punished with electric shock or LiCl injections after killing and eating crickets. Control mice received saline injections, delayed shock, or delayed LiCl injections after attacking and eating crickets. LiCl injections and electric shock were both effective in suppressing cricket killing and eating. It is reported that shock suppressed both attack and eating responses, while LiCl injections suppressed eating responses more than attack responses. 12 references. (Author abstract)

002425 Kostas, Jeanne. University of Kentucky **Effects of psychotropic agents on spontaneous alternation in rats neonatally exposed to lead-acetate. (Ph.D. dissertation).** Dissertation Abstracts International. 39(6):3035-B, 1978. Ann Arbor, Univ. Microfilms No. 7824406, 119p., 1977.

The effects of several psychotropic drugs in rats neonatally exposed to lead via maternal milk were behaviorally evaluated by means of spontaneous alternation testing in the Y-maze and exploration in the open field. Spontaneous alternation in the Y-maze proved to be a measure that was sensitive to both the effects of lead treatment and the interaction of the lead treatment with certain drugs. Toxic effects of lead are characterized by behavioral deficits and altered responses to psychotropic agents at a level sufficiently low enough to preclude more overt toxicological signs. Psychotropic agents investigated include: amphetamine, deanol, imipramine, and apomorphine. (Journal abstract modified)

002426 Kuhn, D. M.; White, F. J.; Appel, J. B. Section on Biochemical Pharmacology, NHLBI, NIH, Bethesda, MD 20014 **The discriminative stimulus properties of LSD: mechanisms of action.** Neuropharmacology (Oxford). 17(4/5):257-263, 1978.

Male Sprague-Dawley rats were trained to discriminate 0.08mg/kg D-lysergic acid diethylamide (LSD) from saline in a two lever operant procedure. After reliable stimulus control was established, rats were tested with various drugs that alter the functional activity of transmitter containing neuronal systems. L-tryptophan, chlorimipramine, and fluoxetine (which increase the synaptic availability of serotonin) neither blocked nor mimicked LSD. Quipazine, a putative agonist, produced an almost complete (78%) transfer to LSD. The presumed serotonin antagoists methiopen, 2-bromo-D-lysergic acid diethylamide, methysergide, cyproheptadine, and cinanserin blocked the LSD cue in a dose related manner. The potent dopamine antagonists haloperidol, fluphenazine, trifluoperazine, alpha-flupenthixol, and ()-butaclamol had no effect on the discriminability of LSD; alpha-adrenergic, beta-adrenergic, cholinergic, and histaminergic antagonists were also without effect. Apomorphine, a dopamine agonist, produced a partial transfer to LSD. Results indicate that the discriminative stimulus properties of LSD may be mediated by postsynaptic serotonin or LSD receptors, with no apparent involvement of dopamine receptors. 45 references. (Author abstract modified)

002427 LaBella, Frank; Havlicek, Viktor; Pinsky, Carl; Leybin, Leonid. Dept. of Pharmacology and Therapeutics, University of Manitoba, Faculty of Medicine, Winnipeg, Manitoba, Canada R3E OW3 **Opiate-like, naloxone-reversible effects of androsterone sulfate in rats.** Canadian Journal of Physiology and Pharmacology (Ottawa). 56(6):940-944, 1978.

Androsterone sulfate(5alpha-androstan-3alpha-ol-17-one, 3-sodium sulfate) administered to freely moving male Sprague-Dawley rats via cerebroventricular cannulae elicited responses similar to those produced by certain opiate drugs and by the endogenous peptide beta-endorphin. These effects included wet dog shakes, body jerks, rigidity, Straub tail, hypermotility, excessive grooming, hyperreactivity to stimuli, aggression, escape behavior, EEG spiking, and behavioral and EEG seizures. These effects appeared during the 5 minute infusion period, persisted in some cases for several hours, and were diminished by pretreatment with the narcotic antagonist naloxone. Results sug-

gest that steroid hormones and opiate compounds act upon some of the same central pathways. 18 references. (Author abstract modified)

002428 Larue-Achagiotis, Christiane; Le Magnen, Jacques. Lab. Neurophysiologie Sensorielle et Comportementale, College de France, 11, place Marcelin Berthelot F-75231 Paris Cedex 05, France **The different effects of continuous night and day-time insulin infusion on the meal pattern of normal rats: comparison with the meal pattern of hyperphagic hypothalamic rats.** Physiology & Behavior. 22(3):435-439, 1979.

The effects of continuous intravenous infusion of insulin on the meal patterns of male Wistar rats were examined. During the day, a dose response curve was apparent; an 86-220% increase in the 12 hour cumulative intake was due to an increase in the number of meals for the lowest dose and in both the size and number of meals for the highest dose. When the same doses of insulin were given at night, the average increase in 12 hour intake was only 27% and the increases were not dose dependent. The changes in meal pattern seen under the effects of continuous insulin infusion were similar to those observed after ventromedial hyothalamic lesions, suggesting that hyperinsulinism play a role in hypothalamic hyperphagia. 24 references. (Author abstract modified)

002429 Lees, A. J.; Fernando, J. C. R.; Curzon, G. Dept. of Neurochemistry, Institute of Neurology, 33 John's Mews, London WC1N 2NS, England **Serotonergic involvement in behavioural responses to amphetamine at high dosage.** Neuropharmacology (Oxford). 18(2):153-158, 1979.

Administration of 15mg/kg ip d-amphetamine to male Sprague-Dawley rats increased normal motor activity (forward locomotion and rearing) and stereotyped behavior (head swaying and gnawing). Amphetamine also produced some abnormal motor behavior (backward locomotion and circling); this behavior was enhanced by administration of the serotonin (5-HT) precursor tryptophan and decreased by the 5-HT synthesis inhibitor p-chlorophenylalanine, the 5-HT receptor blockers metergoline and cyproheptadine, the 5-HT uptake inhibitor fluoxetine, and the dopamine receptor blocker alpha-flupenthixol. This, the backward locomotion and circling appear to be activated by dopamine and 5-HT released by d-amphetamine at high doses; normal motor activities and stereotyped gnawing appear to be activated by dopamine and inhibited by 5-HT. 22 references. (Author abstract modified)

002430 Lloyd, Mary Anne; Appel, James B.; McGowan, William T., III. Alternatives, 1516 Pine Ave. West, Montreal, Quebec, Canada **Effects of morphine and chlorpromazine on the detection of shock.** Research Report, NIMH Grant MH-24333, 1978. 23 p.

The extent to which the perceptual effects of compounds such as morphine and chlorpromazine (CPZ) can be attributed to drug-induced changes in the ability to detect shock stimuli was studied using a discrete trial, two choice, ""yes/no" procedure in rats. Drug effects were analyzed on five measures of performance with multivariate statistical procedures. Both morphine and CPZ at varying doses significantly reduced overall accuracy. Morphine effects were somewhat greater than CPZ, particularly at lowest shock intensity. When compared to appropriate sabine control days, morphine but not CPZ significantly reduced discrimination accuracy on trials when shocks were presented, whereas CPZ but not morphine reduced accuracy on no shock trials. Qualitative differences between the two compounds were observed with respect to shock intensity. Both compounds increased times to initiate trials and to make choice responses with qualitative differences in drug effects. It is concluded that an inverse relationship existed between effects of shock intensity and morphine, and a direct relationship existed between effects of CPZ and shock intensity. 19 references. (Author abstract modified)

002431 London, Edythe Danick. University of Maryland Baltimore Professional Schools **Electroshock convulsant patterns and thresholds in neonatal rats: influence of monoamine reduction. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 7800666, HC$15. MF$7.50. 93 p. 1976.

The importance of brain monoamines in regulating motor patterns and thresholds to electroshock convulsions in neonatal rats was assessed to obtain information about involvement of specific monoamines in mechanisms that regulate seizure discharge. The characteristic motor response of neonatal rats to 6Hz and 60 Hz minimal and maximal electroshock were observed throughout postnatal development. Effects of tetrabenazine, reserpine on electroshock thresholds, and of 6-hydroxydopamine or p-chloroamohetamined on maximal convulsions produced by 60 Hz electroshock were observed. Effects of all drugs on steady state concentrations of norepinephrine, dopamine and serotonin were assessed. It was concluded that 1) monoaminergic systems limit responses to electroshock in neonatal rats, and are functional as early as day one; 2) clonic convulsions in response to 60 Hz electroshock stimulation involve additional neuronal systems which do not participate in low frequency electroshock convulsions; 3) in neonatal rats, monoamines limit propagation of seizure activity; 4) catecholamines regulate the maximal electroshock threshold in neonatal rats; 5) the developing nervous system adapts to catecholamine deficiency in relation to electroshock convulsant thresholds. (Journal abstract modified)

002432 Lorden, Joan F. University of Alabama at Birmingham, Birmingham, AL 35233 **Neurochemical influences on taste aversion learning. (Unpublished paper).** Final Report, NIMH Grant RO3-MH-30389, 1978. 7 p.

The extent and nature of involvement of central catecholamine and indoleamine systems in the acquisition of learned aversions were investigated in albino rats. Emphasis was on the role of catecholamine systems in the blocking effectiveness of chemical neurotoxins and the effects of raphe lesions upon taste aversion learning. The results indicate that central monoamine systems participate in this type of learning in a variety of ways. Depletion of central monoamines can affect both acquisition and extinction in the conditioned aversion paradigm, depending on the system damaged and the drug used to induce the aversion. Clearcut differences in the sites of two related drugs (amphetamine and fenfluramine) were also demonstrated.

002433 Lynch, Marina A.; Kenny, Marie; Leonard, B. E. Pharmacology Department, University College, Galway, Ireland **Effect of d-amphetamine on the behavior of rats in the open field apparatus: interaction with four neuroleptics and changes in biogenic amine metabolism in discrete brain regions.** Irish Journal of Medical Science (Dublin). 147(10):337-350, 1978.

The effects of a single dose of d-amphetamines on the concentration of biogenic amines and their precursors in the rat brain were investigated. An acute dose of d-amphetamine caused marked stereotyped licking, sniffing, and gnawing, and hyperactivity. These effects were prevented by chlorpromazine. It was found that the amphetamine induced change in dopamine metabolism in both the striatum and olfactory lobes returned to control levels following chlorpromazine treatment. It is suggested that the behavioral changes induced by amphetamine are a consequence of changes in dopamine metabolism in both the striatum and mesolimbic systems. The acute administration of

amphetamine also caused an increase in concentration of tryptophan and 5-HT in the brainstem, striatum, and some regions of the limbic system. 5-HT may play an ancillary role in amphetamine-induced behavioral changes. In the chronic study, d-amphetamine sulphate was added to the drinking water of rats in increasing concentrations over a period of 14 days. An assessment of the behavior of the animals was made in the open-field apparatus during the period of drug administration and for up to 6 days after withdrawal. It is concluded that the chronic amphetamine test may be of some value in the elucidation of potential neuroleptics, particularly those with a thioridazine profile. 41 references. (Author abstract modified)

002434 Lynch, Marina A.; Leonard, B. E. 30(12):798-799, 1978. **Effect of chronic amphetamine administration on the behaviour of rats in the open field apparatus: reversal of post-withdrawal depression by two antidepressants.** Journal of Pharmacy and Pharmacology (London). Pharmacology Department, University College, Galway, Ireland

The effects of amitriptyline and mianserine on the depression of open field activity induced in male Wistar rats by withdrawal of amphetamine after chronic treatment were examined. Ambulation scores increased throughout the 21 day period of amphetamine administration, while rearing and grooming scores were not significantly altered. Following withdrawal of the drug, a marked decrease in ambulation and rearing scores and an initial increase in grooming behavior were observed. Administration of mianserin for 4 days partially reversed the depression of ambulation and rearing in withdrawn rats. In constrast, treatment with amitriptyline for 6 days after amphetamine withdrawal had no effect on behavior. It is suggested that this amphetamine withdrawal model of depression may be useful in screening potential antidepressants with mechanisms of action unlike those of the tricyclic antidepressants. 8 references.

002435 Marsden, C. A.; Curzon, G. Dept. of Physiology and Pharmacology, Medical School, Queen's Medical Centre, Nottingham, NG7 2UH, England **The role of tryptamine in the behavioural effects of tranylcypromine L-tryptophan.** Neuropharmacology (Oxford). 18(2):159-164, 1979.

The effects of reduced tryptamine synthesis on the behavioral syndrome induced by L-tryptophan (100mg/kg) in male Sprague-Dawley rats pretreated with the monoamine oxidase inhibitor tranylcypromine (20mg/kg) were examined. Two inhibitors of brain L-amino acid decarboxylase, 5-aminooxymethyl-2-bromophenol (NSD-1055, 50mg/kg) and DL-serine 2(2,3,4-trihydroxybenzyl)-hydrazine hydrochloride (R04-4602, 300mg/kg), were given, so that the accumulation of tryptamine in the brains of rats given L-tryptophan after tranylcypromine was markedly reduced, but levels of brain 5-hydroxytryptamine (5-HT), striatal dopamine, and hypothalamic noradrenaline were only slightly altered. Hyperactivity was reduced and the behavioral syndrome was prevented by R04-4602, but tryptamine (2.5mg/kg) restored the syndrome. NSD-1055 reduced the hyperactivity and greatly reduced the behavioral syndrome. Since the complete behavioral syndrome could also be produced by 5-hydroxytryptophan and tranylcypromine, these results suggest that tryptamine has an important role in the behavioral effects of tryptophan/tranylcypromine but may act in part by releasing 5-HT. 21 references. (Author abstract modified)

002436 Martin, G. E.; Haubrich, D. R. Merck Institute for Therapeutic Research, West Point, PA 19486 **Striatal dopamine release and contraversive rotation elicited by intranigrally applied muscimol.** Nature (London). 275(5677):230-231, 1978.

The effect of muscimol, a potent gamma-aminobutyric acid (GABA) agonist, on striatal dopamine matabolism and release was studied to clarify the action of GABA on the nigrostriatal dopaminergic system. Intraperitoneally administered muscimol was found to increase the concentration of striatal homovanillic acid, and the intranigral perfusion of muscimol was found to evoke simultaneously both contraversive turning and dopamine release from the ipsilateral striatum of rats. These findings support the hypothesis that muscimol-evoked turning and striatal dopamine release are causally related and suggest that striatal dopamine mediates the turning. Muscimol may act to release dopaminergic neurones from tonic inhibition mediated by other substantia nigra neurotransmitters. Further studies of the effects of muscimol on these substances may help to determine the precise mechanism whereby intranigrally administered muscimol evokes both contraversive turning and striatal dopamine release. 25 references.

002437 Martinez, Joe L., Jr.; Vasquez, Beatriz J.; Jensen, Robert A.; Soumireu-Mourat, Bernard; McGaugh, James L. Dept. of Psychobiology, School of Biological Sciences, University of California, Irvine, CA 92717 **ACTH4-9 analog (ORG 2766) facilitates acquisition of an inhibitory avoidance response in rats.** Pharmacology Biochemistry and Behavior. 10(1):145-147, 1979.

The effects of ORG 2766, an analog of the adrenocorticotrophic hormone fragment ACTH4-9, on inhibitory avoidance behavior in Fischer 344 rats were investigated. Graded doses of ORG 2766 were administered 1 hour prior to training, immediately after training, or 1 hour prior to the 24 hour retention test. A 5.0mg/kg dose of ORG 2766 administered prior to training significantly facilitated acqusition of the response. ORG 2766 did not significantly affect retention when administered after training or prior to the retention test. Since ORG 2766 only affected acquisition of the response, it is suggested that the drug acts by influencing sensory, motivational, or attentional variables rather than by directly affecting memory consolidation or retrieval processes. 11 references. (Author abstract modified)

002438 Mason, Stephen T.; Fibiger, Hans C. Division of Neurological Sciences, Department of Psychiatry, University of British Columbia, Vancouver, BC, V6T 1W5, Canada **The dorsal bundle extinction effect: dependence on subtle changes in acquisition.** Brain Research (Amsterdam). 166(2):341-348, 1979.

Destruction of the ascending noradrenergic innervation to the forebrain in male Woodlyn rats by intracerebral injection of 6-hydroxydopamine (4mcg in 2mcl, injected bilaterally into the dorsal bundle in the mesencephalon) caused resistance to extinction of a continuously reinforced lever-press response. However, this effect occurred only if the lesion was present during acquisition training on the reinforced schedule; no resistance to extinction was seen in rats lesioned after the completion of acquisition training, just prior to the extinction phase. Thus, the behavioral effect that manifests itself during extinction appears to be due to subtle changes in the acquisition learning process. This is consistent with the prediction of an attentional theory of noradrenergic function and excludes most other suggested explanations of the dorsal bundle extinction effect. 33 references. (Author abstract modified)

002439 McCoy, Daniel J.; Brown, Daniel J.; Forney, Robert B. Department of Toxicology, Indiana University School of Medicine, Indianapolis, IN 46202 **The effect of cannabinoid mixtures on induced sleep intervals and the disappearance of ethanol and hexobarbital.** Research Communications in Psychology, Psychiatry and Behavior. 3(2):89-99, 1978.

The combined effects of cannabidiol (CBD) and delta9-tetrahydrocannabinol (THC) on ethanol and hexobarbital-in-

duced sleep intervals were investigated in male Swiss Webster mice. THC was observed to lengthen both ethanol and hexobarbital-induced sleep. CBD lengthened only sleep induced by hexobarbital. CBD and THC mixture produced a synergistic lengthening of hexobarbital-induced sleep. Ethanol disappearance was not changed by any pretreatment. CBD, however, alone and in combination with THC, blocked the disappearance of hexobarbital. THC had no effects on this disappearance. It is concluded that the effects of THC within the experimental parameters measured are mediated by a central mechanism, while the effects of CBD are produced by a metabolic blocking mechanism. The synergistic interaction of CBD and THC on hexobarbital sleep, coupled with the lack of alteration of hexobarbital disappearance, support previous evidence indicating a central action of THC which would produce effects whether present, alone, or in combination with CBD. 9 references. (Author abstract modified)

002440 McGuire, J. L.; Awouters, F.; Niemegeers, C. J. E. Ortho Pharmaceutical Corporation, Raritan, NJ 08869 **Interaction of loperamide and diphenoxylate with ethanol and methohexital.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 236(1):51-59, 1978.

The antidiarrheal drugs loperamide and diphenoxylate were tested for their ability to potentiate central nervous system depression induced by ethanol in mice and methohexital in rats. Oral diphenoxylate potentiated the loss of righting reflex (hypnosis) in mice and rats at doses which were considerably lower than those required to induce morphine-like behavior in mice and rats. Oral loperamide did not potentiate hypnosis. It is concluded that the failure of loperamide to potentiate the action of hypnotics confirms data from clinical trials which showed that loperamide is essentially free of central depressant effects when given orally. 22 references. (Author abstract modified)

002441 McGuire, Patricia S.; Seiden, Lewis S. Dept. of Pharmacological and Physiological Sciences, University of Chicago, 947 East 58th Street, Chicago, IL 60637 **The effects of tricyclic antidepressants on a differential reinforcement of low-rates schedule in rats. (Unpublished paper).** Research Report, NIMH Grant MH-11191, 1978. 35 p.

Rats performing on a differential reinforcement of low rates 18 sec (DRL18) schedule of water reinforcement were administered imipramine, desmethylimipramine, or chlorimipramine in an investigation of the effects of tricyclic antidepressants on response rates. Doses of 2.5mg/kg to 10.0mg/kg imipramine and desmethylimipramine produced a decrease in response rate and an increase in reinforcement rate. To determine whether this decrease in response rate and increase in reinforcement rate was related to the anticholinergic properties of the tricyclics, scopolamine, a cholinergic blocker, was also tested on a DRL18 schedule. Scopolamine increased responses, decreased reinforcements, and increased interresponse times shorter than 18 sec. 35 references. (Author abstract modified)

002442 McKearney, James W.; Barrett, James E. Worcester Foundation for Experimental Biology, Shrewsbury, MA 01545 **Schedule-controlled behavior and the effects of drugs.** In: Blackman, D., Contemporary research in behavioral pharmacology. New York, Plenum, 1978. 506 p. (p. 1-68).

Reinforcement and punishment are discussed in terms of basic determinants of behavior and determinants of the effects of experimental interventions such as the administration of drugs. Focus is placed on a variety of related factors that can influence both the effects of new environmental events and the effects of drugs on animal behavior. These include: 1) characteristics of presently ongoing behavior, 2) that behavior's antecedents and consequences, 3) the subjects's prior experience, and 4) the total environmental context in which behavior occurs. Topics discussed include: reinforcement schedules, noxious stimuli, the effects of drugs on schedule controlled behavior, response rate as a determinant of the behavioral effects of drugs, the effects of drugs on behaviors maintained by different events, and the effects of drugs on punished responding. It is felt that the effects of drugs on behavior is as complex as the multiple ways in which behavior is determined. 103 references.

002443 McLaughlin, Carol L.; Baile, Clifton A. Department of Clinical Studies, School of Veterinary Medicine, University of Pennsylvania, Kennett Square, PA 19348 **Cholecystokinin, amphetamine and diazepam and feeding in lean and obese Zucker rats.** Pharmacology Biochemistry and Behavior. 10(1):87-93, 1979.

In a study of the control of food intake in Zucker fatty rats, the gastrointestinal hormone cholecystokinin (CCK) was injected into lean and fatty, reduced and nonreduced littermates. The fatty rats were less sensitive than lean rats to ip injections of 20Ukg CCK after a 6 hour fast and fatty rats were less sensitive to 5U/kg CCK when reduced than when obese. The fatty rats were as sensitive as lean rats to injections of 0.5and 1.0mg/kg d-amphetamine sulfate, but they were less sensitive when reduced. Injections of 1.25 and 2.5mg/kg diazepam produced smaller increases in food intake after a 6 hour fast in fatty and reduced fatty rats than in lean rats. Combination treatment with CCK and diazepam in fatty and lean rats produced feeding behavior similar to that following injection of vehicle. Diazepam and amphetamine had additive effects in fatty and lean rats, but the fatty rats appeared to be more sensitive to amphetamine than to diazepam. Results indicate that the Zucker fatty rat is less sensitive than lean rats to chemicals that affect food intake, supporting the contention that its CNS is generally less responsive. 35 references. (Author abstract modified)

002444 Meeker, R. B.; Myers, R. D. Department of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Patterns of food intake in the monkey during free or restricted feeding and in response to 2-DG or insulin injection.** Physiology & Behavior. 22(3):563-574, 1979.

The feeding patterns of restrained macaque monkeys and the effects of alterations in glucose metabolism on these patterns were investigated. When given free access to food, the monkeys established a pattern of ingestion characterized by frequent meals and a stable caloric intake of 26-33g/kg/day. When the availability of food was restricted to 8 hours per day, the number of meals decreased, but the mean daily intake and the size of the first meal increased. A subcutaneous injection of 300mg/kg 2-deoxy-D-glucose (2-DG) caused a 100% increase in the size of the first meal, a reduction in the number of meals, and no change in daily food intake; the compensatory adjustment to the large first meal was made through a decrease in the number of meals eaten, with the insertion of one extremely long postmeal interval. Insulin (1.0or 5.0U/kg) evoked an increase in the size of the first meal and in daily food intake, but only in the female macaque; the failure to regulate caloric intake accurately was due to an increase in the magnitude of two or more meals. The differential patterning of food intake after 2-DG results in greater satiation than normal, whereas a meal consumed during insulin-induced hypoglycemia may be less satiating. 30 references. (Author abstract modified)

002445 Mello, Nancy K.; Mendelson, Jack H. Alcohol and Drug Abuse Research Center, McLean Hospital, 115 Mill Street, Belmont, MA 02178 **Self-administration of an enkephalin analog by rhesus monkey.** Pharmacology Biochemistry and Behavior. 9(5):579-586, 1978.

In a study of self-administration of an enkephalin analog by rhesus monkeys, intravenous injections of the synthetic pentapeptide, FK-33-824, were found to maintain operant responding under second order schedule control (FR 4 (VR 16:S)) in five, morphine dependent rhesus monkeys. All monkeys self-administered enkephalin in amounts equivalent to morphine at comparable doses per injection. No monkey developed opiate withdrawal signs during 56 hours of enkephalin substitution except at the lowest enkephalin dose. These data attest to the reinforcing characteristics of an enkephalin analog in rhesus monkey and suggest that natural polypeptides may contribute to the reinforcing properties of opiate drugs. 37 references. (Author abstract modified)

002446 Menon, M. K.; Clark, W. G. Psychopharmacology Research Laboratory, Veterans Administration Medical Center, Sepulveda, CA 91343 **GABA-ergic drugs block the locomotor stimulant effects of 1,3-dimethyl-5-aminoadamantane (D-145).** Neuropharmacology (Oxford). 18(2):223-225, 1979.

The gamma-aminobutyric acid (GABA) agonists muscimol and 4,5,6,7-tetrahydroisoxazolo (S,4-c) pyridin-3-ol hydrate (THIP) blocked the locomotor stimulation produced by 1,3-dimethyl-5-aminoadamantane (D-145) in male Swiss mice, with THIP about three times less potent than muscimol. Both drugs were less effective as antagonists of d-amphetamine-induced motor excitation. In mice pretreated with aminooxyacetic acid (AOAA), maximum blockade of the D-145 induced stimulation was observed in 3 and 6 hour AOAA pretreatment groups; the blockade seen in 2 and 8 hour pretreatment groups was significant but weaker. It is suggested that D-145 produces locomotor stimulation via GABA antagonistic effects in specific brain areas, most likely the dopamine rich basal ganglia structures. 10 references. (Author abstract modified)

002447 Messiha, F. S. Department of Pathology, Psychopharmacology Laboratory, Texas Tech University School of Medicine, Lubbock, TX 79409 **Voluntary drinking of ethanol by the rat: biogenic amines and possible underlying mechanism.** Pharmacology Biochemistry and Behavior. 9(3):379-384, 1978.

The relationship between biogenic amine metabolite produced changes in voluntary drinking of ethyl alcohol (ET) solution by the rat, as well as their in vivo effects on the enzymes primarily involved in the hepatic metabolism of ET, i.e. liver alcohol (L-ADH) and aldehyde dehydrogenase (L-ALDH), was investigated. Administration of vanillylmandelic acid, 5-hydroxyindoleacetic acid, and homovanillic acid markedly reduced ET drinking. Similar effects occurred after administration of neutral metabolites of the biogenic amines, after injection of metanephrine or 3-methoxy-4-hydroxyphenylpyruvic acid. Threodihydroxyphenylserine, but not L-dopa, reduced ET intake. Treatement with peripheral decarboxylase inhibitors significantly reduced ET drinking as contrasted with nonsignificant decline in consumption following benserazide. Short-term administration of the compounds produced varied effects on L-ADH and L-ALDH. It is suggested that alteration of hepatic ADH by the compounds might account for the observed reduced ET drinking, thereby indicating the contribution of pheriphral sources rather than central factors in mediating the behavioral effects. 37 references. (Author abstract modified)

002448 Milar, Katharine S.; Halgren, Carl R.; Heise, George A. University of North Carolina, Chapel Hill, NC 27514 **A reappraisal of scopolamine effects on inhibition.** Pharmacology Biochemistry and Behavior. 9(3):307-313, 1978.

The effects of scopolamine on discrimination performance in the presence or absence of a stimulus signaling nonreiforcement were studied. In Experiment 1, rats trained to respond on one of two levers in the presence of a 1000 Hz tone and on the other lever in the presence of a 3000 Hz tone were not reinforced when white noise was added to one of the tones. Pairing white noise with the other tone during an extinction session demonstrated that the white noise had become a conditioned inhibitory stimulus. In Experiment 2, scopolamine decreased responding and discrimination accuracy on the excitatory (reinforced) trials and increased responding on the inhibitory (nonreinforced) trials. The magnitude of the drug's effect was similar on excitatory and inhibitory trials. Using combinations of visual and auditory discriminative stimuli, Experiment 3 confirmed the results of Experiment 2. These experiments show that scopolamine disrupts animals' ability to discriminate, and that scopolamine-induced increases in nonrewarded responses cannot be attributed solely to a disinhibitory effect of the drug as Carlton (1969) and others have claimed. 21 references. (Author abstract)

002449 Moore, Frank L. Dept. of Zoology, Oregon State University, Corvallis, OR 97331 **Differential effects of testosterone plus dihydrotestosterone on male courtship of castrated newts, Taricha granulosa.** Hormones and Behavior. 11(2):202-208, 1978.

Sexually responsive Taricha granulosa males were castrated and implanted with testosterone (T), dihydrotestosterone (DHT), T plus DHT, or no steroid, and courtship behavior was observed. The incidence of sexual behavior was highest in castrates implanted with T plus DHT. Newts implanted with T or DHT exhibited sexual behavior more frequently than did the untreated castrates, which exhibited none during the last 5 days of testing. A second experiment was conducted using sexually unresponsive males. The occurrence of sexual behavior remained low in castrates implanted with T plus DHT, untreated castrates, and intact control males. These results support the hypothesis that for these species of amphibian the presence of adequate levels of testicular androgen is a necessary, but not sufficient, condition for the manifestation of sexual behavior; the appearance of these behaviors requires, in addition, the presence of some nontesticular hormone. 19 references. (Author abstract modified)

002450 Mormede, P.; Dantzer, R. I.N.R.A., Station de Pharmacologie-Toxicologie, 180, Chem de Tournefeuille, F-31300, Toulouse, France **Pituitary-adrenal influences on avoidance behavior of pigs.** Hormones and Behavior. 10(3):285-297, 1978.

Effects of ACTH and dexamethasone (DX) on aspects of avoidance conditiioning in pigs were examined. Pigs submitted to extinction of a signaled conditioned avoidance response were injected daily with various doses of DX or ACTH. Pigs treated with 0.2mg/kg of DX showed a higher number of intertrial crosses, but the extinction rate was not modified by either treatment. Effects of ACTH and DX were further studied on the reaction to a Pavlovian conditioned fear signal presented to pigs having learned a continuous avoidance response in a shuttle box. DX treatment before both the fear conditioning and the test sessions enhanced the reaction to the fear signal at intermediate doses but had little effect at lower and higher doses. ACTH 1-24 treatment induced the same behavioral changes as intermediate doses of DX. Results demonstrate that, in pigs, avoidance performance changes under fear signal presentations are modulated by corticosteroids. 33 references. (Author abstract modified)

002451 Murphy, James Michael. Bowling Green State University **The role of catecholamines in the mediation of starvation- and amphetamine-induced locomotor arousal in mice. (Ph.D. dissertation).** Dissertation Abstracts International. 39(5):2562-B, 1978. Ann Arbor, Univ. Microfilms No. 7819864, 160p., 1978.

The role of dopamine (DA) and norepinephrine (NE) systems in the control of locomotor arousal, with an emphasis on the behavioral arousal accompanying food deprivation, was studied in three experiments. The first experiment demonstrates the viability of a daily 2-hour test which measures starvation-induced locomotor arousal in mice. Locomotor activity peaks on the third day of total food deprivation at nearly three times ad lib control levels. It is observed that the primary mechanism of increased activity is a failure of food deprived animals to habituate to the test environment. Experiment 2 shows that food deprivation-induced locomotor arousal is dependent upon NE systems, as pretreatment with dopamine-beta-hydroxylase inhibitor FLA-63 attenuates activity of food deprived mice to near control levels. Experiment 3 compared the role of DA and NE systems in locomotor arousal which accompanies food deprivation, and amphetamine, to determine if arousal response occurs by a similar activation of catecholamines (CAs) in each case. Results show both CAs are important in control of locomotor activity and arousal. Blocking agents for DA or NE systems considerably decrease locomotor activity in control, food deprivation, and amphetamine conditions. Results demonstrate the necessity of both CA systems for locomotor activity and arousal. A particular balance of CA activation is important for the locomotor arousal following amphetamine administration, although NE systems have greater importance in directing arousal toward locomotor expression. (Journal abstract modified)

002452 Najjar, Salem E.; Blake, Martin I.; Benoit, Philippe A.; Lu, Matthias C. College of Pharmacy, University of Illinois Medical Center, Chicago, IL 60680 **Effects of deuteration on locomotor activity of amphetamine.** Journal of Medicinal Chemistry. 21(6):555-558, 1978.

The synthesis of fully deuterated amphetamine (phenyl-2-aminopropane-d11) in which 11 deuterium atoms are bonded to carbons and two other highly deuterated analogues, is described. Their toxicities and in vivo spontaneous locomotor activities in mice were examined and compared with that of the parent protioamphetamine. A significant reduction in toxicities and a decrease in spontaneous locomotor activities were observed for these highly enriched deuterated analogues, as compared to protioamphetamine. 15 references. (Author abstract)

002453 Nandy, Kalidas. Geriatic Center, V. A. Hospital, Bedford, MA **Centrophenoxine and the aging mammalian brain.** Gerontological Society: 31st Annual Scientific Meeting. 18(5, Part 2):106, 1978.

A summary of a paper read at the 31st Annual Meeting of the Gerontological Society, held in Dallas, November 1978, is presented. The effects of centrophenoxine on the learning and memory of old mice were studied and the results correlated with change in the neuronal lipofuscin pigment. Eleven to 12 month old female mice were treated with centrophenoxine for 12 weeks and their learning and memory were tested in a T-maze. The number of trials required to attain the criterion in 20 treated old mice were compared with those of 20 untreated mice of the same age, and for 20 younger, untreated mice. It was noted that the treated mice learned with significantly fewer trials than than the control animals. Lipofuscin pigment was visualized by its characteristic autofloruescence, histochemical staining with PAS and Nile blue sulfate and electron microscopy. Treatment with centrophenoxine caused a significant reduction of the lipofuscin pigment in the neurons of the cerebral cortex and hippocampus compared to the control group of the same age. (Author abstract modified)

002454 Nicak, A.; Kohut, A. Dept. of Pharmacology, Medical Faculty, University P. J. Safarik, Kosice, Czechoslovakia **Development of tolerance to morphine and pethidine in rats in dependence on age.** Activitas Nervosa Superior (Praha). 20(3):231-235, 1978.

The development of tolerance to the analgesic effect of morphine (10 mg/kg i.p.)and to pethidine (40mg/kg i.p.)given every 3 hours 13 times in succession or every 6 or 24 hours 7 times in succession was studied in Wistar rats of different age groups (21 days, 42 days, 3 months, and 18 months). Pain threshold was determined by electric algic stimulation. The rate of tolerance development to the analgesic effect of morphine and pethidine decreased with age and changed only slightly with the frequency of application. In young animals (21 days old) the analgesic effect was very intensive after the first application of pethidine as well as morphine, but after further applications the analgesic effect was reduced sharply until it completely disappeared. In animals aged 42 days and 3 months the analgesic effect was not so strong after the first application but the decrease too was slower. In 18-months-old animals the analgesic effect after the first dose was high and declined moderately after further doses. It is assumed that the development of tolerance to the effect of strong analgesics is related to the rate of protein synthesis of the central nervous system. 12 references. (Author abstract)

002455 Niemegeers, C. J. E.; Janssen, P. A. J. Dept. of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340, Beerse, Belgium **In vivo interaction of haloperidol and apomorphine.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 236(1):43-50, 1978.

The effects of apomorphine and haloperidol on motility were measured in rats using a Doppler method. With respect to solvent treated rats, apomorphine increased and haloperidol decreased the motility counts. When both compounds were given in combination, a mutually dose related antagonism was found indicative for a competitive interaction. The ratio between apormorphine and halperidol producing normal motility over a wide dose range was 27.6:1. This ratio corresponds to the differences in receptor affinity in vitro of these compounds and thus appears to be the consequence of competitive binding at dopaminergic receptor sites. It is concluded that this mutual antagonism may thus serve as a model for the concept of individualized dosage in haloperidol therapy for schizophrenia and mania. 35 references. (Author abstract modified)

002456 Nock, Bruce; Feder, Harvey H. Institute of Animal Behavior, Rutgers University, Newark, NY 07102 **Noradrenergic transmission and female sexual behavior of guinea pigs.** Brain Research (Amsterdam). 166(2):369-380, 1979.

Treatment with the dopamine-beta-hydroxylase inhibitor U-14,624 (50, 100, or 150mg/kg) blocked the induction of lordosis behavior by estradiol benzoate (EB) and progesterone (P) in ovariectomized guinea pigs. After treatment with U-14,524 (100mg/kg), the norepinephrine (NE) content of the medial basal hypothalamus, preoptic area, and cortex was reduced by 55% and the dopamine (DA) content of the medial basal hypothalamus was increased by 155% during the period when females treated with EB and P normally display lordosis. Treatment with the NE receptor stimulator clonidine (1.0mg/kg) restored lordosis behavior in females treated with EB, P, and U-14,624, but the putative DA and serotonin (5-HT) receptor blockers, pimozide (1.0mg/kg) and methysergide (20.0mg/kg), were ineffective in this respect. Thus, U-14,624 appeared to inhibit lordosis primarily by reducing NE neurotransmission rather than by increasing DA or 5-HT activity. Pretreatment with the postsynaptic alpha-adrenergic antagonist phenoxybenzamine (20.0mg/kg) blocked the facilitation of lordosis by clonidine in females primed with EB alone or EB plus P, suggesting that the facilitatory effects of clonidine on lordosis are mediated

by activation of postsynaptic alpha-adrenergic receptors. 26 references. (Author abstract modified)

002457 Nomura, Yasuyuki; Segawa, Tomio. Dept. of Pharmacology, Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine, Kasumi 1-2-3, Hiroshima 734, Japan **Apomorphine-induced locomotor stimulation in developing rats treated with 6-hydroxydopa.** European Journal of Pharmacology (Amsterdam). 50(2):153-156, 1978.

Apomorphine-induced locomotor stimulation was investigated in developing Wistar rats injected with 6-hydroxydopa at birth. The treated animals showed enhanced responsiveness to apomorphine at 20 days, but were less sensitive to the drug than controls at 30 days. Apomorphine again elicited more locomotor stimulation in 6-hydroxydopa treated animals than in controls on day 50. Results suggest that the altered sensitivity of dopamine receptors induced with 6-hydroxydopa is influenced by the onset of activity of other inhibitory neurons on day 30. 12 references. (Author abstract modified)

002458 Numan, Michael. Dept. of Psychology, Boston College, Chestnut Hill, MA 02167 **Progesterone inhibition of maternal behavior in the rat.** Hormones and Behavior. 11(2):209-231, 1978.

A series of experiments investigating the role of progesterone in inhibiting the onset of maternal behavior in the rat is described. Female rats hysterectomized and ovariectomized on day 16 of pregnancy and injected subcutaneously with 20 microgram/kg of estradiol benzoate (EB) show a short latency to onset of maternal behavior when presented with test pups 48 hr later. A subcutaneous injection of either 1mg or 5mg of progesterone on day 16 of pregnancy and again 24 hr later inhibited this EB-induced short latency onset of maternal behavior. The central neural site at which progesterone might act to produce this inhibitory effect was explored. Female rats, hysterectomized and ovariectomized on day 16 of pregnancy and injected subcutaneously with EB, received implants of crystalline progesterone on day 16 of pregnancy into either the medial preoptic area, ventromedial hypothalamus, midbrain tegmentum, dorsal raphe nucleus, or median raphe nucleus. No inhibitory effects were found and all females showed a short latency onset of maternal behavior. Several possible explanations for this lack of inhibitory effect of intracerebral implantation of progesterone are discussed. 37 references. (Author abstract)

002459 Olson, Gayle A.; Olson, Richard D.; Kastin, Abba J.; Castellanos, F. Xavier; Kneale, Mary T.; Coy, David H.; Wolf, Robert H. Dept. of Psychology, University of New Orleans, New Orleans, LA 70122 **Behavioral effects of D-Ala2-beta-endorphin in squirrel monkeys.** Pharmacology Biochemistry and Behavior. 9(5):687-691, 1978.

The effects of D-Ala2-beta-endorphin administered either intravenously (IV) or intracisternally (IC) in squirrel monkeys were tested using a number of behavioral measures: general activity, eating, social behavior, aggression/distress, analgesia, and startle/escape. Every monkey was tested with all tasks on each of five identical repeated trials, one preinjection baseline trial and four postinjection trials. After IC administration, the two largest doses exerted toxic effects, which were partially reversed with naloxone, producing in two cases muscular rigidity and profound sedation. The small (4mcg/kg) dose produced significant decreases in activity over trials but increased reactivity to noxious stimulation after the initial postinjection trial. Results demonstrate significant behavioral effects of an endorphin analog in the squirrel monkey after both central and peripheral injection. 16 references. (Author abstract modified)

002460 Paden, Charles McKenzie. University of Colorado, Boulder **Metabolic kinetics of newly synthesized and total dopamine in the neostriatum of the rat. (Ph.D. dissertation).** Dissertation Abstracts International. 39(5):2563-B, 1978. Ann Arbor, Univ. Microfilms No. 7820545, 283p., 1978.

To determine whether neurotransmitter dopamine exists in multiple metabolic compartments within the rat neostriatum, newly synthesized dopamine was radiolabeled by intravenous injection of tritiated L-tyrosine into 8-week-old male Fisher 344 rats. Dopamine synthesis was inhibited 10 minutes later by intraperitoneal injection of alpha-methyl-p-tyrosine (AMPT) and rats were then sacrificed by exposure to microwave radiation at various intervals. Levels of tritiated dopamine and tyrosine, and total dopamine and tyrosine were determined in each animal. Results from analysis of the rates of change of total and radiolabeled dopamine levels reveal no significant differences between behavior of newly synthesized and total dopamine. Results indicate that newly synthesized dopamine is not preferentially catabolized as predicted by multiple pool models, and that the biphasic decline of neostriatal dopamine following treatment with AMPT does not arise from the monoexponential decay of dopamine from two independent compartments. The experiment was repeated following the intravenous injection of the neuroleptic haloperidol 5 minutes prior to the administration of tritiated tyrosine. This treatment results in an approximately fivefold increase in the rate of neostriatal dopamine synthesis. Results from these experiments suggest that neostriatal dopamine metabolism is a single compartment of transmitter possessing rapidly variable rate constants of synthesis and catabolism. (Journal abstract modified)

002461 Palfai, Tibor. no address /**The behavioral and biochemical correlates of pentylenetetrazol (PTZ) and reserpine-induced amnesia and effects of PTZ and reserpine on whole brain biogenic amines. (Unpublished paper).**/ no title. Final Report, NIMH Grant MH-26800, 1978. 7 p.

The effects of pentylenetetrazol (PTZ), reserpine, l-dopa, d,l,5-hydroxytryptophan (d,l,5-HTP), and dihydroxyphenylserine (DOPS) on memory formation and whole brain biogenic amines were determined. It was found that only convulsive doses of PTZ produced retrograde retention impairment but the impairment was not due to state dependent learning; readministration of reserpine before retention testing further impaired retention of both a discrimination and passive avoidance task. Experiments on the effects of the drug treatments on whole brain norepinephrine (NE) and 3,4-dihydroxyphenethylamine (DA) indicate that reserpine produces a time dependent decrease in these amine levels. The data imply that correlating whole brain catecholamine levels with the probability of memory formation may not be a fruitful path of investigation. 9 references.

002462 Panksepp, Jaak; Herman, Barbara; Conner, Robert; Bishop, Paul; Scott, J. P. Department of Psychology, Bowling Green State University, Bowling Green, OH 43403 **The biology of social attachments: opiates alleviate separation distress.** Biological Psychiatry. 13(5):607-618, 1978.

The possiblity that brain opiate systems participate in the control of social affect was assessed by determining the capacity of low doses of exogenous opiates to reduce distress vocalizations of socially isolated puppies. Low doses of opiates were capable of profoundly reducing crying as well as the motor agitation they exhibit during brief periods of social isolation. Since reductions in crying could be obtained with morphine in the absence of any gross behavioral disturbances, the possibility is entertained that brain opiates may function to control the intensity of emotions arising from social separation. Possible parallels between the biological nature of narcotic addiction and the forma-

tion of social bonds are discussed. 20 references. (Author abstract)

002463 Parker, Lorne Fredrick. University of Washington **Conditioned tolerance to the narcotic effects of ethanol in rats. (Ph.D. dissertation.)** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 7800962, HC$15. MF$7.50. 99 p. 1977.

In a series of three experiments, the role of conditioning in mediating the development of tolerance to the narcotic effects of ethanol was examined. In the first experiment rats were given large intraperitoneal doses of ethanol (4g/kg bodyweight) just prior to being placed in a unique environment composed of a plastic chamber permeated with the odor of mentholatum for 10 such conditioning trials. They were then administered large doses of ethanol on 2 consecutive days, and the duration of loss of righting reflexes than controls. Thus the development of tolerance to ethanol's narcotic effects was mediated entirely by conditioning. In the remaining two experiments, the dose response characteristics of ethanol tolerance development were examined with conditioning trials similar to the first experiment, but conditioning trials were given for 26 days. Both experiments' results demonstrate that the low dose group showed a greater conditioned response than the high dose group and that the conditioned ethanol tolerance could be extinguished. The results support a unitary theory of drug tolerance and dependence based on conditioning. (Journal abstract modified)

002464 Parrott, R. F. A.R.C. Institute of Animal Physiology, Babraham, Cambridgeshire, England **Courtship and copulation in prepubertally castrated male sheep (Wethers) treated with 17beta-estradiol, aromatizable androgens, or dihydrotestosterone.** Hormones and Behavior. 11(1):20-27, 1978.

The effects of propionated testosterone, dihydrotestosterone, 19-hydroxytestosterone, and 17beta-estradiol on the development of courtship and copulation in prepubertal castrated sheep were compared. Sheep were castrated the day after birth, and four animals were in each treatment group. Treatments were in the form of subcutaneous injections given 5 days per week over a 6 week period during which time individual animals were observed in 18 tests for sexual behavior. The stimulus females were ovariectomized ewes maintained in a state of continuous receptivity by daily injections of 15mg testosterone propionate. Various measures of sexual and aggressive behavior were recorded during each test. Mounting was induced mainly in animals in the testosterone propionate group and to a lesser extent in those receiving estradiol dipropionate. The extent to which precopulatory courtship was induced decreased according to the following order: testosterone propionate; estradiol dipropionate; 19-hydroxy-17, 19-dipropionate. Animals treated with dihydrotestosterone propionate or arachis oil showed negligible sexual activity. 26 references. (Author abstract modified)

002465 Pert, Agu; Dewald, Louise A.; Gallager, Dorothy W. Biological Psychiatry Branch, National Institute of Mental Health, Bethesda, MD 20014 **Effects of opiates on nigrostriatal dopaminergic activity: electrophysiological and behavioral analyses. (Unpublished paper).** Bethesda, MD, NIMH, 1978. 3 p.

The actions of opiate on dopamine (DA) activity in the substantia nigra (SN) were investigated. In rats lesioned unilaterally in the SN with 6-OHDA, chronically administered morphine produced rotational behavior ipsilateral to the lesion. Direct injections of opiates into the SN-induced rotational behavior contralateral to the injection. Iontophoretic studies, however, failed to reveal any effects of morphine on DA neurons. Thus, while opiates in the SN activate DA neurons, this activation appears to be indirect. 16 references. (Author abstract)

002466 Petersen, Stewart. Dept. of Physiology, University of Leicester, University Road, Leicester LE1 7RH, England **Effects of testosterone upon feeding in male mice.** Animal Behaviour (London). 26(3):945-952, 1978.

The effects of testosterone upon feeding in C57 mice were examined by recording food intake and pattern of feeding in intact and castrate male mice. Intact adults were larger and ate more than prepubertal castrates, due to rapid growth at puberty. Castration in adulthood had little effect upon food intake, but feeding became concentrated into large, infrequent meals. The change in meal size appeared primary and was reversed by testosterone. During rapid growth at puberty, both meal size and frequency were high. Results suggest that testosterone affects feeding in two ways. Rapid weight gain in puberty leads to high meal size and frequency, but in adulthood meal size was depressed. Meal size in adults was further depressed by stimuli from females, and it is argued that testosterone affects a general mechanism for altering feeding when other activities have a high priority. 9 references. (Author abstract modified)

002467 Pieri, Margherita; Schaffner, R.; Pieri, L.; Da Prada, M.; Haefely, W. F. Hoffmann-La Roche & Co., Ltd., Pharmaceutical Research Department, CH-4002 Basel, Switzerland **Turning in MFB-lesioned rats and antagonism of neuroleptic-induced catalepsy after lisuride and LSD.** Life Sciences. 22(18):1615-1622, 1978.

The effects of lisuride, a d-lysergic acid diethyl amide (LSD) and apomorphine were studied in rats with unilateral destruction of nigrostriatal nerve terminals either with 6-hydroxydopamine (6-OHDA) or 5,6-dihydroxytryptamine (5,6-DHT). Lisuride induced contralateral turning for more than 4 hours, while the circling induced by LSD and apomorphine persisted for only 1 hour. Lisuride, a compound stimulating both dopamine and 5-hydroxytryptamine (5-HT) receptors induced a more intense turning in 6-OHDA than in 5,6-DHT lesioned rats. This might indicate a modulation of 5-HT on rotational behavior. Haloperidol antagonized both lisuride and LSD-induced turning. LSD, and much more persistently lisuride, counteracted the prochlorperazine-induced catalepsy. The findings correlate with the biochemical data, indicating that lisuride is a potent agonist at central dopaminergic receptors. 28 references. (Author abstract)

002468 Poling, Alan; Appel, James B. Department of Psychology, University of South Carolina, Columbia, SC 29208 **Drug effects under automaintenance and negative automaintenance procedures.** Pharmacology Biochemistry and Behavior. 9(3):315-318, 1978.

To study the effects of psychotropic drugs under automaintenance conditions, three food deprived pigeons were initially exposed to an automaintenance procedure in which brief periods of response key illumination were followed by food delivery without regard to behavior. Keypecking occurred at a high rate while the key was illuminated and was reduced in dose dependent fashion by acute administration of 0.05-0.45mg/kg LSD, 1.0-8.0mg/kg quipazine, 0.08-0.32mg/kg haloperidol, and 4.0-16.0mg/kg pentobarbital. Ss were then exposed to a negative automaintenance procedure in which food delivery followed key illumination only if the lighted key was not contacted. Keypecking occurred at a low rate under this procedure, with no responses occurring during the majority of key illuminations and was decreased or unaffected by LSD, quipazine, and haloperidol. Pentobarbital increased responding at doses of 4.0mg/kg and 8.0mg/kg and reduced responding at a dose of 16.0mg/kg. 24 references. (Author abstract modified)

002469 Prado de Carvalho, L.; Izquierdo, I. Disciplina de Neurofisiologia, Departamento de Biofisica e Fisiologia, Escola Paulista de Medicina, 04023 Sao Paulo, SP, Brazil **Electroencephalographic and behavioral observations in rats during chronic ethanol ingestion and after abstinence.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 235(2):280-288, 1978.

The electroencephalographic and behavioral effects of chronic ethanol ingestion and after abstinence were examined in rats given increasing aqueous solutions of ethanol beginning after weaning. A 12% v/v concentration was reached on day 81 postpartum and then maintained. Animals drinking 12% ethanol had a median blood alcohol level of 333mg/1. No major changes in hippocampal or neocortical EEG patterns were observed at age 3.5or 6 to 7 months old, during the ingestion phase. Upon withdrawal, the younger group showed a decline of the mean frequency of hippocampal and neocortical large, irregular EEG activity; in contrast, the older group showed a decline in the frequency of EEG theta. The performance of pseudoconditioned and conditioned shuttle responses was unaltered after 3.5to 6 months of ethanol consumption or after 1 week's abstinence. 22 references. (Author abstract modified)

002470 Pycock, C. J.; Horton, R. W.; Carter, C. J. Dept. of Pharmacology, Medical School, University of Bristol, Bristol BS8 1TD, England **Interactions of 5-hydroxytryptamine and gamma-aminobutyric acid with dopamine.** Advances in Biochemical Psychopharmacology. 19:323-341, 1978.

The biochemical and behavioral interactions between 5-hydroxytryptamine (5-HT) gamma-aminobutyric acid (GABA) and dopamine (DA) are discussed. Pharmacological studies in laboratory animals indicate that both 5-HT and GABA exert inhibitory influences on DA function. Studies of drug-induced catalepsy and hyperactivity suggest a reciprocal balance between 5-HT and DA and between GABA and DA. These transmitter functional interactions suggest that neurological orders related to DA dysfunction (Parkinson's disease, dyskinesias, and psychoses) may be treated with agents other than the classic dopaminergic drugs. 70 references.

002471 Quock, Raymond M.; Weick, Barton G. Dept. of Physiology-Pharmacology, School of Pharmacy, University of the Pacific, Stockton, CA 95211 **p-Chloroamphetamine-induced hyperthermia pharmacologically distinct from fenfluramine-induced hyperthermia.** Journal of Pharmacy and Pharmacology (London). 31(1):27-32, 1979.

The mechanisms underlying hyperthermic responses to p-chloroamphetamine (PCA) and fenfluramine were examined in male New Zealand rabbits. PCA evoked hyperthermia, behavioral excitation, and prominent forepaw clonic activity, whereas fenfluramine produced only hyperthermia and behavioral stimulation. Responses to both agents were reduced by the 5-hydroxytryptamine (5-HT) uptake inhibitor, fluoxetine; potentiated by the monoamine oxidase inhibitor, pheniprazine; and unaltered by the dopaminergic antagonist, haloperidol. Pretreatment with the 5-HT receptor blockers cinanserin, cyproheptadine, or D-2-bromolysergic acid diethylamide markedly attenuated the effects of fenfluramine, but only slightly influenced responses to PCA. Depletion of central 5-HT stores with p-chlorophenylalanine also affected responses to fenfluramine more than those to PCA. The tryptaminergic receptor blocker methergoline abolished the hyperthermia and forepaw clonus, but not the behavioral stimulation, induced by PCA; fenfluramine effects were only partially reduced by methergoline. Results suggest that fenfluramine responses may be mediated by 5-HT, while the PCA responses may be mediated by tryptamine. 42 references. (Author abstract modified)

002472 Ramabadran, K.; Jacob, J. J. C. Laboratory of Pharmacology, Pasteur Institute, 28, rue du Docteur Roux, F-75724, Paris Cedex 15, France **Facilitatory effect of naloxone and involvement of specific ligand-opiate receptor system in the antinociceptive effects of non-opioid drugs.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 236(1):27-42, 1978.

Interactions of naloxone with neuroleptics, cholinergic agonists, and miscellaneous drugs were examined using male Swiss mice. The facilitatory effects exerted by naloxone on a nociceptive reaction (jumping) in the hot plate test were not modified by three phosphodiesterase inhibitors, and were not diminished by neuroleptics or cholinergic agonists. Naloxone antagonized the antinociceptive effects of neuroleptics in different patterns. The antagonism by the opioid antagonists of the antinociceptive effects of cholinergic agonists appeared to be of a competitive type. It is concluded that the facilitatory effects of naloxone did not apparently involve activation of adenyl cyclase or the mediation of dopaminergic or cholinergic (neural) structures. 87 references. (Author abstract modified)

002473 Randall, P. K.; Amaral, P.; Ringering, L. S. Andrus Gerontology Center, University of Southern California, Los Angeles, CA 90007 **Effects of chronic neuroleptics on catalepsy and stereotypic behavior in aging mice.** Gerontological Society: 31st Annual Scientific Meeting. 18(5, Part 2):114, 1978.

A summary of a paper read at the 31st Annual Meeting of the Gerontological Society, held in Dallas, November 1978, is presented. The cataleptic response to haloperidol and the sterotypic response to a direct dopamine agonist were investigated in male C57B1/6J mice at 3, 9, and 24 months of age following 21 days of daily i.p. injection of 1.5mg/kg haloperidol or equal volumes of the vehicle. Three and 9-month-old animals showed reductions in duration of the cataleptic response and increased sensitivty to apomorphine, while the 24-month-old animals increased response time to haloperidol and failed to alter their sensitivity to apomorphine as a result of the chronic treatment. In addition, a large increment in catalepsy was observed in 24-month-old animals receiving chronic vehicle injection, indicating a possible interaction of stress of handling and injection with the neuroleptic which was confined to the older group. Findings suggested that in addition to possible decrements in basal receptor function indicated by diminished striatal binding of antagonist ligands, aging animals were less able to show compensatory increases in receptor function as a result of long-term receptor blockade. (Author abstract modified)

002474 Reinstein, Daniel K.; McClearn, Duane; Isaacson, Robert L. Dept. of Psychology, University of Florida, Gainesville, FL 32611 **The development of responsiveness to dopaminergic agonists.** Brain Research (Amsterdam). 150(1):216-223, 1978.

The ontogenetic development of the behavioral effects of apomorphine and ET-495 was studied in Long-Evans hooded rats to evaluate the systems specific effects on the two dopamine (DA) systems hypothesized by Cools and his coworkers (1976). It was hypothesized that if there were specific effects on two distinct systems, that 1) either distinct patterns of behaviors would evolve at different rates in response to the drugs over development, or 2) similar patterns evolving at two distinct rates would be observed with ET-495-induced effects preceding the apomorphine effects. Results suggest that the histochemical distinctions used by others to define the development of two DA systems may not correlate directly with behavior. In addition to the two DA systems defined by their origins and projection pathways, there may exist distinct DA sensitive subsystems that are responsible for the mediation of specific behaviors. 25 references.

002475 Rezek, M.; Havlicek, V.; Leybin, L.; **LaBella, F. S.**; Friesen, H. Dept. of Physiology, Faculty of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada R3E W3 **Opiate-like naloxone-reversible actions of somatostatin given intracerebrally.** Canadian Journal of Physiology and Pharmacology (Ottawa). 56(2):227-231, 1978.

The possibility that the effect of central administration of somatostatin (SRIF) might be mediated through opiate receptors was tested on rats pretreated with the opiate receptor blocker naloxone. The latency to tail flick response in the rat was significantly prolonged by cerebroventricular infusion of 1.0microgram of SRIF and more so with 10.0micrograms. The D-tryptophan analog was less effective than native SRIF. Pretreatment with naloxone eliminated analgesia, but not seizures induced by SRIF. Recording of the electroencephalographic activity enabled determination of the specific state of the sleep/waking cycle in which the repeated tail flick responses were tested. Latency was generally longer in both control and test animals when tail immersion was performed during the state of sleep or drowsiness, rather than during the awake state. Although animals receiving SRIF were less likely to fall asleep between subsequent test trials, the average latency was actually longer than after control saline infusion when the animals slept more. SRIF, unlike other releasing factors and peptides tested, showed significant activity in an opiate radioreceptor assay. The blockade of SRIF action by naloxone pretreatment, along with binding of SRIF to opiate receptors in vitro, suggested that opiate receptors are involved in the mediation of the observed analgesia. 12 references. (Author abstract modified)

002476 Riffee, William H.; Wilcox, Richard E.; **Smith, Robert V.** Dept. of Pharmacology and Drug Dynamics Institute, College of Pharmacy, University of Texas, Austin, TX 78712 **Comparison of behavior arousal induced by apomorphine and N-n-propylnorapomorphine.** Research Communications in Chemical Pathology and Pharmacology. 22(2):301-312, 1978.

A preliminary evaluation of behavioral arousal in mice induced by apomorphine (APO) and N-n-propylnorapomorphine, (NPA) as a model system for quantifying activity of presumptive antiparkinsonian and antischizophrenic agents, was made. As measured by electromagnetic sensors, behavioral arousal reflects several responses including spontaneous locomotor activity and repetitive movements (e. g.,grooming and rearing). Results show that for a 90 min period over the 1mg to 10mg dose range employed, APO exhibits a linear dose response relationship whereas that for NPA is sigmoidal. Similarities in time of peak effect and ED50s for the two aporphines in stereotypic cage climbing and behavioral arousal experiments suggest that the behavioral arousal-inuced by APO and NPA may be dopaminergically mediated. 7 references. (Author abstract modified)

002477 Riffee, William H.; Wilcox, Richard E.; **Smith, Robert V.** Dept. of Pharmacology, College of Pharmacy, University of Texas, Austin, TX 78712 **Stereotypic and hypothermic effects of apomorphine and N-n-propylnorapomorphine in mice.** European Journal of Pharmacology (Amsterdam). 54(3):273-277, 1979.

The dopaminergic agonists apomorphine (APO) and N-n-propylnorapomorphine (NPA) produced significant hypothermia and stereotypic cage climbing in male CD-1 mice. Dose/response analyses (0.5-10mg/kg ip) indicated that on a milligram basis, the two drugs induced similar magnitudes of stereotypic behavior. Similar analyses of drug-induced hypothermia (0.008-40mg/kg ip) indicated that NPA was approximately 90 times as potent as APO. These results suggest that two different types of dopaminergic systems may be responsible for the hypothermic and stereotypic responses observed. 14 references. (Author abstract modified)

002478 Rodgers, Charles H. Biological Laboratories, Department of Psychiatry, University of Illinois Medical School, Chicago, IL 60612 **Influences of retrochiasmatic surgical transection on mating and serum ovarian hormone levels in the androgenized rat.** Hormones and Behavior. 11(1):110-122, 1978.

The effect of surgical transections in the retrochiasmatic area (FC) on the incidence of mating in androgenized rats was studied, and the relationship of mating behavior to serum levels of ovarian hormones was examined. Four of 31 rats treated with testosterone propionate (TP) showed minimal mating without surgery, and 27 failed to mate. Mating occurred up to 30 days following FC, whereas temporary mating, resulting from sham FC, declined to presurgical levels within 30 days after surgery. Mating after ovariectomy was not facilitated by daily injections of .2mcg of estradiol cypionate, but was facilitated after daily injections of 1.6mcg. TP treated rats with FC showed more mating after 1.6mcg estradiol cypionate than did sham FC and controls not treated with TP. Serum estradiol-17beta and progesterone levels at autopsy did not differ between TP treated rats mating without surgery and those failing to mate. Serum levels of estradiol-17beta did not differ between controls and FC rats, although serum progesterone levels were decreased in the FC group. These findings confirm that neonatal androgen treatment may produce central nervous system changes causing deficits in mating in the adult animal. It is suggested that androgen-induced central nervous system changes result in a more sustained inhibitory input to the mediobasal hypothalamus than is present in the animal not treated with TP. 22 references. (Author abstract modified)

002479 Rodgers, R. J. Postgraduate School of Psychology, University of Bradford, Bradford, England **Influence of intra-amygdaloid opiate injections on shock thresholds, tail-flick latencies and open field behaviour in rats.** Brain Research (Amsterdam). 153(1):211-216, 1978.

The hypothesized limbic motivational/affective control of pain suggested by Melzack and Casey was investigated. It was demonstrated that while corticomedial amygdaloid injection of morphine elevates aversive thresholds of Sprague-Dawley rats on a shock motivated test (tail flick) and decreases open-field emotionality, similar injections fail to alter a spinal reflex to pain or open-field activity. Results suggest an altered state of emotional reactivity in rats injected with morphine in the corticomedial amygdala. It is suggested that these injections may indirectly attenuate emotional responsiveness to aversive stimulation by producing a state of euphoria incompatible with aversive responding. 21 references.

002480 Rosen, J. Tel Aviv University, Tel Aviv, Israel **Learning under metrazol-induced wave-spike discharges in rats.** Israel Journal of Medical Sciences (Jerusalem). 14(9):1004-1005, 1978.

A summary of a paper presented at the 41st Meeting of the Israel Physiological and Pharmacological Society, held March 1978, in Jeruselam is presented. The mechanisms of learning deficits were examined. This was accomplished by using a passive conditioning task during metrazole-induced wave-spike (WS) discharges and later testing the acquisition in a drug free state. Female albino rats with chronically implanted electrodes over the visual cortex were either injected i.p. with metrazole or an equivalent amount of saline. Half the Ss received stroboscopic flashes. In the metrazole group, flashes were given only during WS discharges. The following day, this same flash was paired with footshock. Rats receiving preexposed flashes performed significantly worse than the controls as revealed by a drinking suppression test. Metrazole groups did not perform differently than their respective saline controls. These results strongly suggest that experimental WS discharges may not

impair learning and memory mechanisms but rather that the disturbance is in the ability to perform required motor movements. (Author abstract modified)

002481 Russell, Roger W.; Macri, James. Macri: Dept. of Pharmacology, University of California, Los Angeles, CA **Central cholinergic involvement in behavioral hyper-reactivity.** Pharmacology Biochemistry and Behavior. 10(1):43-48, 1979.

The hypothesis that behavioral reactivity to changes in environmental stimulation varies concomitantly with changes in the cholinergic system was tested in male Sprague-Dawley rats. Acute reduction of acetylcholine (ACh) levels was achieved by intracerebronventricular injection of hemicholinium-3 (HC-3), and chronic ACh reduction was obtained with electrolytic lesions of the septum. Significant and quantitatively equivalent hyperreactivity occurred when rats were exposed to a variety of stimulus changes at peak effect times for the acute and chronic experimental treatments. However, during noncontingent shock stimulation, the septal animals were significantly hyperreactive, but the HC-3 rats were not. Results are discussed in relation to the imbalance hypothesis of affective disorders, which states that mania reflects decreased cholinergic activity relative to catecholoaminergic or indoleaminergic activity, whereas depression reflects an imbalance in the opposite direction. 44 references. (Author abstract modified)

002482 Sahakian, B. J.; Growdon, J. H.; Millington, W. R.; Barr, J. K.; Wurtman, R. J. Laboratory of Neuroendocrine Regulation, Dept. of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, MA 02139 **The effects of cholinergic agonists on apomorphine-induced stereotyped behavior in the rat.** Communications in Psychopharmacology. 2(3):255-262, 1978.

To examine the involvement of cholinergic synapses in apomorphine-induced stereotyped behavior, the intensity of stereotypy in rats given both apomorphine and a direct (pilocarpine, RS-86, arecoline) or indirect (physostigmine, choline chloride) cholinergic agonist was rated. Pilocarpine and RS-86 antagonized apomorphine-induced stereotypy but arecoline did not. Neither agent acutely raised striatal acetylcholine levels. Physostigmine significantly elevated striatal acetylcholine levels but did not antagonize the stereotypy. Higher doses suppressed stereotyped behavior but also produced tremor and immobility. Choline chloride significantly raised acetylcholine levels in the striatum but did not antagonize the stereotypy. It is concluded that direct stimulation of striatal muscarinic receptors can suppress apomorphine-induced stereotypyed behavior without necessarily affecting striatal acetylcholine levels. Indirectly acting cholinergic agonists increase striatal acetylcholine levels but lack an immediate effect on stereotypy. 26 references. (Author abstract modified)

002483 Sanberg, Paul R.; Pisa, Michele; Fibiger, Hans C. Division of Neurological Sciences, Department of Psychiatry, University of British Columbia, Vancouver, BC, Canada, V6T 1W5 **Avoidance, operant and locomotor behavior in rats with neostriatal injections of kainic acid.** Pharmacology Biochemistry and Behavior. 10(1):137-144, 1979.

Compared with saline injected controls, male Wistar rats with bilateral injections of kainic acid (KA) in the dorsal neostriatum showed increased locomotor response to d-amphetamine, increased resistance to extinction, and impaired acquisition and retention to passive avoidance. The KA injection resulted in a loss of local neurons in the dorsal neostriatum; with no appreciable damage to dopaminergic terminals or to extrinsic myelinated axons, thus confirming the selective neurotoxic action of KA on neuronal perikarya and the proposed similarity of KA-induced neostriatal lesions with those found in the caudate putamen of patients with Huntington's disease. Loss of hippocampal neurons was occasionally observed, but the behavioral results could not be wholly attributed to hippocampal damage; rats with no demonstrable extrastriatal lesions were not less impaired than those with hippocampal damage. It is suggested that an altered arousal reaction to stressful situations may account for the learning and memory impairments of the KA lesioned rats. 55 references. (Author abstract modified)

002484 Sansone, M. Laboratorio di Psicobiologia e Psicofarmacologia, CNR, 1, via Reno I-00198 Rome, Italy **Effects of chlordiazepoxide-scopolamine combinations on shuttle-box avoidance performance of mice.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 235(1):93-102, 1978.

When given separately during training in the shuttlebox or in trained male CD-1 mice, chlordiazepoxide and scopolamine improved avoidance responding. Avoidance facilitation was much more evident, especially in the initial phases of training, when the two drugs were combined. Results suggest that the two drugs, especially in combination, may produce state dependence phenomena consisting of an asymmetrical dissociation of learning. 24 references. (Author abstract modified)

002485 Sato, M.; Hikasa, N.; Otsuki, S. Okayama University, Japan **Effects of nomifensine and imipramine on amygdaloid kindled convulsion -- inhibitory effects of dopamine on epileptic seizure.** Psychiatria et Neurologia Japonica (Tokyo). 80(7):425-428, 1978.

The effects of nomifensine and imipramine on amygdaloid kindled convulsion was studied in cats, focusing on the inhibitory effects of dopamine on epileptic seizure. In cats with experimentally-induced generalized convulsions, the antidepressive agent nomifensine had an anticonvulsant action when administered in small nontoxic doses. At higher doses, nomifensine did not act as an anticonvulsant. The tricyclic antidepressive agent imipramine had no anticonvulsant action. Results suggest that while imipramine and nomifensine both block noradrenaline turnover in the brain, nomifensine also acts against dopamine turnover. 6 references.

002486 Scheel-Krugr, J.; Arnt, J.; Braestrup, C.; Christensen, A. V.; Cools, A. R.; Magelund, G. Pharmacological Research Laboratory, Dept. E, Sct. Hans Hospital Roskilde, Denmark **GABA-dopamine interaction in substantia nigra and nucleus accumbens -- relevance to behavioral stimulation and stereotyped behavior.** Advances in Biochemical Psychopharmacology. 19:343-346, 1978.

Studies of the interaction of gamma-aminobutyric acid (GABA) and dopamine (DA) in the rat substantia nigra pars reticulata (SNR) and nucleus accumbens are reviewed. Injection of the GABA agonist muscimol into the SNR resulted in increased DA synthesis in the neostriatum, suggesting that muscimol inhibits impulse flow in the nigostriatal dopaminergic pathway. Muscimol injected into the nucleus accumbens antagonized the locomotor activity induced by the dopamine agonists ergometrine and apomorphine, but markedly facilitated the stereotyped licking and gnawing induced by apomorphine. Systemic pretreatment with muscimol significantly antagonized apomorphine-induced increases in locomotor activity, but facilitated the stereotyped gnawing-induced increases in locomotor activity, but facilitated the stereotyped gnawing induced by cocaine or methylphenidate. It is concluded that muscimol is able to differentially modify various DA systems or receptors involved in DA dependent locomotor activity and stereotyped behavior. 8 references.

002487 Schenberg, L. C.; Graeff, F. G. Department of Pharmacology, Medical School, 14.100 Ribeirao Preto, S.P., Brazil **Role of the Periaqueductal gray substance in the antianxiety action of benzodiazepines.** Pharmacology Biochemistry and Behavior. 9(3):287-295, 1978.

To study the interactions between serotonergic mechanism and electrical stimulation of the mesencephalic central gray substance, rats were trained to lever press for terminating aversive electric stimuli applied at the Periaqueductal gray and adjoining tectum of the mesencephalon. Experimental sessions consisted of 40 discrete escape trials of a maximum 30 sec duration, separated by 30 sec intervals. Dose effect curves of two tryptamine antagonists (cyproheptadine and methysergide) as well as of the benzodiazepine minor tranquilizer, chlordiazepoxide, on average escape latencies and on frequency distribution of individual latencies were determined. Facilitatory effects of the tryptamine antagonists were noted, suggesting that escape behavior is inhibited by brain tryptaminergic mechanisms. A specific depressant effect of chlordiazepoxide on escape from Periaqueductal gray electrical stimulation suggests that this region may be involved in the antianxiety action of benzodiazepines. 50 references. (Author abstract modified)

002488 Schneiderman, N.; Gavin, W. J.; Gaide, M. S.; Klose, K. J.; Silbret, M. University of Miami, Coral Gables, FL 33124 **Heart rate and blood pressure changes during conditioning and exercise in rhesus monkeys.** Psychophysiology. 15(3):291-292, 1978.

A summary is presented of a report on the interaction of static and dynamic components of exercise upon heartrate (HR) and blood pressure (BP) changes in rhesus monkeys, which was delivered to the Seventeenth Annual Meeting of the Society for Psychophysiological Research, held in Philadelphia, October 1977. Four animals received eight daily test sessions in which four loads, four pull frequencies, and alternate sessions of hexamethonium vs saline were combined using a signal avoidance schedule. Under saline systolic BP varied as a function of both pull frequency and load; diastolic BP varied as a function of load; HR varied as a function of pull frequency and as an interaction of pull frequency and load. Baseline recovery following exercise was more rapid for BP than for HR. Hexamethonium abolished HR but not BP responses. However, it is reported that the BP responses were smaller under hexamethonium than under saline and varied only as a function of load. (Author abstract modified)

002489 Schreiber, Henry Louis, III. Texas Tech University **Maternal behavior and offspring amphetamine response. (Ph.D. dissertation).** Dissertation Abstracts International. 39(5):2557-B, 1978. Ann Arbor, Univ. Microfilms No. 7819900, 249p., 1978.

To examine maternal behavior and offspring amphetamine response, young, primiparous and older, multiparous mothers were exposed to: 1) baskets of actively signaling, cold stressed donor pups; 2) baskets of anesthetized donor pups; or 3) baskets of ping pong balls, during the first week after parturition while the mothers' own offspring remained undisturbed. Maternal behavior was assessed before and during exposure to the baskets, and during the week following exposure to the baskets. Results show that young, primiparous mothers responded to donor pups' distress calls by increasing their caregiving behavior. Both groups responded to anesthetized donor pups as they did to activel signaling pups, except that mothers constructed better rated nests. Following weaning, mothers' male offspring were subjected to six consecutive daily injections of saline, 2.5mg/kg of 5.0mg/kg d-amphetamine 30 plus 5 minutes prior to a 2 minute observation in a Y-maze. Following 4 days of an accelerating drug regimen; subjects were injected with saline, and half of the offspring were tested in the Y-maze in the presence of a novel object, while half were tested in its absence. On the next day, subjects were tested in the Y-maze as before, except that all subjects were injected with 5.0mg/kg d-amphetamine. Results show that: 1) stressed pup cue induced maternal behavior is sufficient to determine responsiveness to d-amphetamine; and 2) mother's age plus parity interacts with the elicitation of stressed pop-cue-induced maternal behavior to produce differential responsiveness to amphetamine in offspring. (Journal abstract modified)

002490 Schrot, John; Boren, John J.; Moerschbaecher, Joseph M.; Simoes/Fontes, Jose Carlos. Behavioral Sciences Dept., Naval Medical Research Institute, Bethesda, MD 20014 **Effects of d-amphetamine and cocaine on repeated acquisition with timeout from avoidance.** Pharmacology Biochemistry and Behavior. 9(5):659-663, 1978.

The acute effects of d-amphetamine and cocaine on a repeated acquisition baseline with timeout from avoidance were investigated in two rats. Each session the animals acquired one of two different three member response sequences. Each sequence member was associated with a different keypress response lever. The first two correct responses of each sequence postponed shock for a fixed period of time. The third correct response initiated a signalled timeout (30 sec) from avoidance. Baseline performance was characterized by a decrease in errors within each session. In comparison to control sessions, both d-amphetamine and cocaine increased errors and altered the pattern of within session acquisition. D-amphetamine increased the rate of sequency completion and the rate of shock delivery in both animals. Cocaine increased the rate of sequency completion in one animal and increased the rate of shock delivery for the other. 12 references. (Author abstract modified)

002491 Semple, James M. Medicinal Research Centre, Cold Harbour Rd. The Pinnacles, Harlow, Essex, CM19 5AD, England **The inhibition of protein synthesis by gluarimide antibiotics and long-term memory.** Irish Journal of Medical Science (Dublin). 147(Supplement 1):63-65, 1978.

A paper read at the first Irish Psychopharmacology Conference, held in Belfast in March 1978, is presented. Research on the effects of gluarimide antibiotics on long-term memory was reviewed. The gluarimide antibiotics, cycloheximide and acetoxycycloheximide, inhibit protein synthesis and have been found to produce performance deficits in fish, birds, and mammals. These performance disruptions may be due to disruption of memory processes, which are mediated by drug effects on protein synthesis. It was concluded that macromolecular synthesis may play a role in the storage of information. 15 references.

002492 Sengstake, Cord B.; Chambers, Kathleen C.; Thrower, James H. Dept. of Psychology, Portland State University, P.O. Box 751, Portland, OR 97207 **Interactive effects of fluid deprivation and testosterone on the expression of a sexually dimorphic conditioned taste aversion.** Journal of Comparative and Physiological Psychology. 92(6):1150-1155, 1978.

The effects of fluid deprivation on the sexually dimorphic rate of extinction of a conditioned taste aversion in rats were investigated. Under ad lib water conditions, males extinguished a conditioned taste aversion more slowly than females. Fluid deprivation increased the rate of extinction of the male but had no effect on the extinction rate of the female. It is proposed that the more rapid extinction rate of the deprived male could be accounted for by a deprivation-induced change in a testosterone dependent mechanism. This proposal is supported by demonstrating that injections of testosterone propionate blocked the effects of fluid deprivation on rate of extinction in the male rat. 15 references. (Author abstract modified)

002493 Setler, Paulette E.; Malesky, Maryann; McDevitt, Joseph; Turner, Katherine. Department of Biological Research, Smith Kline and French Laboratories, Philadelphia, PA 19101 **Rotation produced by administration of dopamine and related substances directly into the supersensitive caudate nucleus.** Life Sciences (Oxford). 23(12):1277-1284, 1978.

Dopamine and related compounds were directly injected into the caudate nucleus in lesion and nonlesioned rats in order to delineate the supersensitivity which underlies dopamine-agonist-induced rotation. Results showed that dopamine, norepinephrine, epinine, epinephrine, apomorphine and 2-amino-6,7-dihydroxytetraline, hydorbromide (ADTN) produce vigorous, long-lasting, dose related contraversive circling. Dopamine was the most potent substance tested, and serotonin produced modest rotation which was not dose related. Piribedil, although more effective than its metabolite S584, produced only a short period of activity at very high doses. Isoproterenol and clonidine were inactive. The supersensitivity of the lesioned rats was manifested as an increase in the potency of dopamine and as an increase in the maximal response, defined as rate of rotation. Rotation was produced in nonlesioned rats only after pretreatment with tranylcypromine, which had no significant effect in lesioned rats. 10 references. (Author abstract modified)

002494 Shavit, Y.; Myslobodsky, M. Tel Aviv University, Tel Aviv, Israel **Rotation behavior and asymmetry of visual-evoked potential in rats.** Israel Journal of Medical Sciences (Jerusalem). 14(9):1005, 1978.

A summary of a paper read at the 41st meeting of the Israel Physiological and Pharmacological Society held March 1978, in Jerusalem is presented. This investigation was designed to see if late components of the bilaterally recorded averaged visual evoked potentials (VEP) show consistent asymmetry in rats displaying rotation behavior. VEP were recorded from chronically implanted extradural electrodes, over symmetrical regions of the visual cortex, in freely moving rats. The direction and amount of turns after administration i.p. of amphetamine were recorded automatically in the rotometer. The most prominent late VEP component, the slow negative wave (SNW) was consistently suppressed in the hemisphere contralateral to the side of rotation. The strength of the side and corresponding motor imbalance in normal rats was recently discovered to be associated with higher dopamine concentration. It is believed that VEP hemispheric asymmetry is an electrophysiological correlate of the dopamine content asymmetry. (Author abstract modified)

002495 Siegel, Harold I.; Rosenblatt, Jay S. Institute of Animal Behavior, Rutgers State University, Newark, NJ 07102 **Duration of estrogen stimulation and progesterone inhibition of maternal behavior in pregnancy-terminated rats.** Hormones and Behavior. 11(1):12-19, 1978.

The duration of the effectiveness of estradiol benzoate (EB) on the latency to the onset of maternal behavior was measured in 16 day pregnant rats that were hysterectomized and ovariectomized (HO). Eight groups of HO animals were treated with either a single subcutaneous injection of 5 mcg/kg of EB or oil at surgery and were initially presented with foster pups at either 24, 48, 72, or 96 hours postoperatively. Compared to their respective controls, EB treated animals showed significantly shorter latencies when testing began at 48 and 72 hours, but not at 24 or 96 hours. In the second experiment, 16 day HO rats were treated with 5 mcg/kg of EB at surgery and either oil or 5mg of progesterone at 0, 24, or 44 hours postoperatively. Additional groups received either progesterone or oil at surgery (instead of EB) and a second injection of oil 44 hours later. Testing began 48 hours following surgery for all groups, and the results showed that only the groups injected with EB alone or EB plus progesterone at 48 hours displayed short latency maternal behavior. It was concluded that a significant reduction in the latency to the onset of maternal behavior can be obtained between 24 and 72 hours after EB treatment, and that progesterone when injected concurrently or 24 hours later can inhibit the effectiveness of EB. 13 references. (Author abstract modified)

002496 Siegel, R. K. Department of Pharmacology, University of California, Los Angeles, CA 90024 **Hallucinogens and attentional dysfunction: a model for drug effects and reality testing.** In: Stillman, R., The psychopharmacology of hallucinogens. New York, Pergamon, 1978. 338 p. (p. 268-296).

A paper read at the workshop on assessing hallucinogenic behavior sponsored by the Division of Research of the National Institute on Drug Abuse in Bethesda, Maryland, December 1976, is presented. The effects of hallucinogens on illusion in monkeys were explored. Four rhesus monkeys were trained in either a color group or a reality group to grasp at real and illusory M&M candies in an apparatus employing a set of two opposing parabolic mirrors. When an object was placed in the bottom mirror, a three dimensional image of the object appeared at a small opening on the top surface of the upper mirror. The following drugs were administered to the subjects in tests of discrimination accuracy: lysergic acid diethylamide, dimethyltryptamine, phencyclidine, scopolamine, delta9-tetrahydrocannabinol, pentobarbital, morphine, chlorpromazine, caffeine, haloperidol, strychnine, bromo-lysergic acid diethylamide, and saline. Results suggest that hallucinogens impair reality discrimination. 99 references.

002497 Siegel, Shepard. Dept. of Psychology, McMaster University, Hamilton, Ontario L8S 4K1, Canada **Tolerance to the hyperthermic effect of morphine in the rat is a learned response.** Journal of Comparative and Physiological Psychology. 92(6):1137-1149, 1978.

Rats were injected with both morphine and physiolgoical saline, with different environment cues associated with each substance, in order to determine the nature of tolerance to the hyperthermic effect of morphine. Results of several experiments indicate that the hyperthermic effect of morphine in rats becomes attenuated over the course of successive administrations by a conditional compensatory, hypothermic response elicited by cues present at the time of morphine administration, thus accounting for hyperthermic tolerance. These findings, implicating a Pavlovian conditioning process in hyperthermic tolerance, are not readily interpretable by tolerance models that do not attribute any role to drug associated environmental cues in the acquisition of tolerance. 52 references. (Author abstract modified)

002498 Slater, P. Department of Physiology, Medical School, University of Manchester, Manchester M13 9PT, England **Effect of tolerance to morphine, ethanol and barbiturate on amphetamine circling in rats with a striatal dopamine lesion.** Journal of Pharmacy and Pharmacology (London). 30(2):88-91, 1978.

The effect of tolerance to morphine, ethanol, and barbital on amphetamine-induced circling in rats with unilateral 6-hydroxydopamine lesions of the nigrostriatal dopamine (DA) projection was investigated in order to determine whether the production of tolerance and physical dependence by these different types of drugs could have common neurochemical features. Amphetamine produced a dose related ipsilateral circling in the lesioned rats. In the morphine dependent animal, the circling rate produced by amphetamine 4 days following morphine pellet implantation was reduced; after naloxone precipitated withdrawal, the amphetamine-induced circling rate increased, returning to control levels after 21 days. In barbital dependent rats, the amphetamine circling response was depressed and remained so

after withdrawal of the drug. In ethanol tolerant animals and following ethanol withdrawal, there was no change in the circling response to amphetamine. The change in the response of striatal DA neurons to amphetamine that occurs after chronic morphine treatment cannot be reproduced with chronic administration of barbital or ethanol. It is concluded that the neurochemical bases of barbiturate and ethanol tolerance are different from that of morphine tolerance. 26 references. (Author abstract modified)

002499 Slifer, Barbara E. Dept. of Psychology, University of Wyoming, Laramie, WY 82071 **Effects of d-amphetamine on schedule-induced escape.** Pharmacology Biochemistry and Behavior. 9(5):609-614, 1978.

In a study of the effects of d-amphetamine on schedule-induced escape, pigeons were trained to respond on a fixed ratio schedule during which 90 responses produced 3 sec of grain reinforcement (FR90). Concurrently, a separate key was available on which a response initated a timeout from the FR schedule and turned off the discriminative stimuli associated with the FR. A second response on the same key terminated the timeout and reinstated the fixed ratio. Pigeons demonstrated a pattern of escape responding immediately following the grain reinforcement. D-amphetamine was administered 30 min before a probe session. Drug effects on a topographically similar response from the same animal during the same session suggest differential effects on schedule-controlled and schedule-induced behavior. 38 references. (Author abstract modified)

002500 Soubrie, P.; Chermat, R.; Poncelet, M.; Simon, P. Departement de Pharmacologie, Faculte de Medecine Pitie-Salpetriere, 91, boulevard de l'Hopital, F-75634 Paris Cedex 13, France **/Models of behavioral inhibition in animals./** Modeles d'inhibition du comportement chez l'animal. Encephale (Paris). 4(5, Supplement):503-511, 1978.

In a paper presented at the Conference on the Concept of Inhibition in Psychiatry, held in Monastir, Yugoslavia, October 1978, different models of behavioral inhibition in animals are examined. It is suggested that the inhibitions induced by fear or anxiety appear as a result of punishment introduction into an unknown situation or frustration. These inhibitions are particularly sensitive to minor tranquilizers. The inhibitions induced by fatigue appear when avoidance situations continue for 24 hours or when a situation demands a marked increase of animal activity to obtain the same reward (food): these inhibitions are particularly sensitive to psychoanaleptics. The inhibition induced by placing an animal in an inescapable situation is particularly sensitive to antidepressants. 3 references. (Journal abstract modified)

002501 Sparber, Sheldon B.; Meyer, Dale R. Department of Pharmacology, 105 Millard Hall, 435 Delaware St., University of Minnesota, Minneapolis, MN 55455 **Clonidine antagonizes naloxone-induced suppression of conditioned behavior and bodyweight loss in morphine-dependent rats.** Pharmacology Biochemistry and Behavior. 9(3):319-325, 1978.

Clonidine's action on naloxone (Nx) induced suppression of fixed-ratio (FR15) responding and bodyweight loss was studied in morphine (M) dependent rats. Clonidine (10 to 70mcg/kg i.p.)injected 30 min prior to the behavioral session resulted in a dose related suppression of operant behavior in M-naive Ss, along with a small but significant decrease in bodyweight at higher doses. More than twice as much weight loss, associated with diarrhea, was obtained when 5.0mg/kg i.p. Nx was administered to M-dependent Ss. When 10 to 50mcg/kg i.p. clonidine was administered prior to Nx in M-dependent Ss, withdrawal induced disruption of operant responding was significantly attenuated. Concurrent weight loss was decreased by as much as 40%. The degree of amelioration of withdrawal appeared inversely related to clonidine dose. The optimal dose was 10mcg/kg which by itself was only partially behaviorally active. The data are discussed in relation to the application of operant techniques for assessing drug treatment designed to alter the severity of narcotic withdrawal. 42 references. (Author abstract modified)

002502 Staudacherova, Dana; Mares, Pavel; Trojan, Stanislav. Institute of Physiology, Faculty of General Medicine, Charles University, Albertov 5, 128 00 Prague 2, Czechoslovakia **Ontogenetic development of pentobarbital-induced EEG pattern and sleeping time in rats.** Developmental Psychobiology. 12(1):11-25, 1979.

The latency of onset and the duration of sleep induced by pentobarbital were examined in albino male rats of the Wistar strain at 9 to 35 days of age, as well as in adult rats. Sleep latency was prolonged and sleep duration shortened with increasing age and maturation. Electrocorticographic (ECoG) changes after pentobarbital administration were studied in rats of 5 to 45 days of age and in adult rats. In rats 9 days of age or less the ECoG manifested only depression of activity, whereas from the 12th day onward all characteristic barbiturate-induced phenomena were registered: spindles, slow waves, and isolated spikes with suppression of background activity. It is concluded that barbiturate spindles could be used as a model for rhythmic thalamocortical phenomena even at early stages of development. 28 references. (Author abstract modified)

002503 Stone, W. E.; Javid, M. J. Department of Physiology, University of Wisconsin Medical School, Madison, WI 53706 **Benzodiazepines and phenobarbital as antagonists of dissimilar chemical convulsants.** Epilepsia. 19(4):361-368, 1978.

Three benzodiazepines and phenobarbital (PB) were tested for their relative potency against seizures induced in mice by chemical convulsants. Convulsants used included pentylenetetrazol (PTZ), 3-mercaptopropionic acid (3-MP), bicuculline, picrotoxin, and isoniazid. Chlordiazepoxide (CDX), diazepam, and nitrazepam were much more effective against PTZ than against 3-MP (a glutamate decarboxylase inhibitor). PB was also more effective against PTZ than 3-MP, but by a much smaller margin. The effectiveness of CDX against four convulsants decreased in the order PTZ, bicuculline, picrotoxin, and 3-MP, while that of PB decreased in the order PTZ, 3-MP, bicuculline, and picrotoxin. CDX was more potent than PB against PTZ, but less potent than PB against 3-MP. CDX was 1.42 and 2.25 times as effective as PB in extending the latent period of isoniazid-induced seizures and antagonizing PTZ-induced seizures, respectively. The claim that benzodiazepines preferentially antagonize seizures associated with a decrease in gamma-aminobutyric acdi (GABA) synthesis is not sustained. Their potent antagonism of PTZ-induced seizures is probably based on a mechanism unrelated to GABA metabolism, release, or action. 26 references. (Author abstract)

002504 Svendsen, Ove. Dept. of Pharmacology and Toxicology, H. Lundbeck & Co. A/S, Ottiliavej 7-9, DK-2500 Valby, Copenhagen, Denmark **Long term effect of teflutixol on apomorphine-induced stereotypy and vomiting in dogs.** European Journal of Pharmacology (Amsterdam). 53(4):387-390, 1979.

Dose/response relationships for apomorphine-induced vomiting and stereotyped running were determined in dogs before and after daily oral treatment with 2.5mg/kg teflutixol for 12 days. The median effective doses for apomorphine-induced vomiting up to 24 days after teflutixol treatment were not significantly different from that obtained before treatment. In contrast, stereotyped running behavior of increasing intensity was

seen 4-12 days after teflutixol treatment; the intensity then declined and returned to normal. Results suggest that the nigroneostriatal dopamine system became hypersensitive after prolonged tefluitixol treatment, while the dopamine receptors of the emetic chemotrigger zone did not. 14 references. (Author abstract modified)

002505 Sweeney, K. F. Dept. of Psychology, Queen's University of Belfast, Belfast, Northern Ireland **The anorectic action of mazindol.** Irish Journal of Medical Science (Dublin). 147(Supplement 1):66-70, 1978.

A paper read at the first Irish Psychopharmacology Conference, held in Belfast in March 1978, is presented. The anorectic action of mazindol, a nonphenylethylamine compound which nevertheless exhibits a biochemical and behavioral profile similar to that of d-amphetamine, was discussed. Pharmacological analysis has implicated a possible role for dopaminergic mediation in the reduction of food intake produced by mazindol. However, side-effects, including changes in general locomotor activity, are important factors to consider in relation to the anorectic activity of pharmacological agents. Mazindol reduces food intake and this effect is antagonized by spiroperidol, a dopamine receptor blocker, even when both agonist and antagonist are given at doses which do not alter locomotor activity. Monitoring the anorectic action of drugs in a free feeding situation, in relation to the distribution of eating and noneating episodes, is suggested as a valuable method for understanding the basis of anorexigenesis. 25 references. (Author abstract modified)

002506 Thiebot, M.-H.; Soubrie, P. INSERM, Unite 19 de Neuropsychopharmacologie, 2 rue d'Alesia, F-75014 Paris, France **Amphetamine-induced circling behavior in rats: effects of unilateral microinjections of GABA and GABA-related drugs into substantia nigra.** Brain Research (Amsterdam). 167(2):307-322, 1979.

To determine whether gamma-aminobutyric acid (GABA) exerts inhibitory control on dopaminergic nigrostriatal neurons, circling behavior was examined in male Wistar AF rats given d-amphetamine (2mg/kg i.p.)45 minutes before unilateral microinjection (0.2mcl/2minutes) into the substantia nigra (SN) of GABA, muscimol, chlordiazepoxide (CDP), or bicuculline. Nonmicroinjected control rats showed spontaneous circling after amphetamine. Saline applied to the SN contralateral to the preferential side of spontaneous rotation enhanced contraversive circling; GABA, CDP, and muscimol counteracted this effect and (except CDP) induced light ipsiversive rotations. When applied to the SN ipsilateral to the preferential side of spontaneous rotations, saline had no marked effect on ipsiversive circling but induced weak contraversive turning; CDP and low concentrations of GABA and muscimol enhanced ipsiversive rotations, higher concentrations of GABA and muscimol transiently decreased ipsiversive circling, and bicuculline induced vigorous contraversive turning. Results indicate that GABA exerts inhibitory control upon dopaminergic nigrostriatal pathways and that CDP exerts GABA-like activity. 49 references. (Author abstract modified)

002507 Thomas, K. V.; Handley, S. L. Pharmacological Laboratories, Dept. of Pharmacy, University of Aston, Birmingham, England **On the mechanism of amphetamine-induced behavioural changes in the mouse. I. An observational analysis of dexamphetamine.** Arzneimittel Forschung (Aulendorf). 28(5):827-833, 1978.

The effects of dexamphetamine were studied in 18 items of observed mouse behavior, assessing intensity of action by scoring differences from control (vehicle injected) mice and by measuring ED50 values for dexamphetamine which cause detectable differences between experimental and control Ss on each item. Results show a clear division of items into two groups according to ED50 values. Group 1 Ss had ED50 values between 1 and 4mg/kg and no changes in whole brain monoamine levels, while Group 2 Ss had values greater than 15mg/kg and reductions in whole brain norepinephrine. Group 1 showed increased motor activity and stereotypes of increased altertness. Group 2 Ss showed compulsive gnawing which was negatively related to most other items, but no evidence occurred for a smooth replacement of one type of activity to another with increasing dose. 21 references. (Author abstract modified)

002508 Thompson, Richard W.; Joseph, Sherry. Western Washington University, Bellingham, WA 98225 **The effect of norepinephrine on tonic immobility in chickens.** Bulletin of the Psychonomic Society. 12(2):123-124, 1978.

The effect of norepinephrine on duration of tonic immobility in chickens was investigated. Cockerel chicks, habituated to the tonic immobility (TI) induction procedure, were tested for TI duration following no injection or injection of saline or norepinephrine. Results indicated that TI duration was an increasing function of norepinephrine dosage level. 4 references. (Author abstract modified)

002509 Thompson, Travis; Glenn, Michael; Winston, Neil; Young, Alice M. Department of Psychology, University of Minnesota, Minneapolis, MN 55455 **Chronic effects of methadone on a line tilt generalization gradient in the pigeon.** Pharmacology Biochemistry and Behavior. 9(3):339-346, 1978.

Using an adjusting interval schedule, pigeons were trained to key peck at a relatively constant rate during 45 degree line tilt presentations and at an extremely low rate in the presence of 0 degree and 90 degree line angles. Subsequently, the birds received intramuscular injections of methadone hydrochloride every 8 hr in doses beginning at 3mg/kg/day and increasing progressively to 90mg/kg/day. Stimulus generalization tests were run on the first day and on the last day a given dose was administered to assess the development of tolerance. Although chronic methadone treatment was associated with an overall decrement in key peck rates, the gradients of line tilt generalization were indistinguishable from saline control gradients at doses as high as 90mg/kg/day. Though the birds exhibited gross behavioral incoordination, visual stimulus control appeared unaffected. 22 references. (Authour abstract)

002510 Tseng, Liang-Fu; Loh, Horace H.; Li, Choh Hao. Department of Pharmacology, University of California, San Francisco, CA 94143 **(D-THR2, THZ5)-enkephalinamide: a potent analgesic by subcutaneous and oral administration.** Life Sciences (Oxford). 23(20):2053-2056, 1978.

Evidence is presented that (D-Thr2, Thz5)-enkephalinamide, administered orally or subcutaneously inhibits the tail flick response to heat stimuli in mice. On a molar basis, this peptide is 1.5to 1.7times more potent an analgesic than morphine by oral administration. 11 references. (Author abstract)

002511 Ungerstedt, Urban; Ljungberg, Tomas; Schultz, Wolfram. Dept. of Histology, Karolinska Institut, S-104 0l Stockholm, 60 Sweden **Dopamine receptor mechanisms: behavioral and electrophysiological studies.** Advances in Biochemical Psychopharmacology. 19:311-321, 1978.

Two aspects of dopaminergic (DA) neurotransmission, the supersensitivity developing after degeneration of presynaptic DA nerve terminals and the postulated existence of different DA receptor populations are discussed. Behavioral and electrophysiological studies indicate that denervation leads to an almost 100 fold increase in sensitivity, but the increase in receptor binding and adenylate cyclase activity does not seem to ac-

count for this large increase. Studies of the behavioral effects of apomorphine indicate the drug can induce either locomotion or delayed gnawing effect, depending on the speed of resorption. Various neuroleptic drugs show striking differences in inhibitng the locomotor and gnawing effects of apomorphine. It is suggested that the induction and inhibition of locomotion and gnawing reflect an action on different presynaptic and postsynaptic DA receptors. 22 references.

002512 Val'dman, A. V.; Kozlovskaya, M. M. Kafedra farmakologii I Leningradskogo meditsinskogo instituta imeni I. P. Pavlova, Leningrad, USSR /**Psychophysiological characteristics of the individual psychotropic activity of benzodiazepine derivatives in experimental conditions.**/ Psikhofiziologicheskaya kharakteristika individual'noy psikhotropnoy aktivnosti benzodiazepinovykh proizvodnykh v usloviyakh eksperimenta. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 78(6):911-919, 1978.

Forty one cats were subjected to a series of 156 experiments in which the hypothalamus was electrically stimulated through implanted electrodes in order to stimulate neurotic states. Under these stressful conditions, and while in an emotionally trying interaction with each other, the cats were given a variety of tranquilizing drugs of the benzodiazepine group: lorazepam, diazepam, chlordiazepoxide, oxazepam, and nirazepam. Significant differences in the effects of these drugs were noted. Lorazepam and diazepam caused a selective and profound tranquilizing effect, eliminated fear and anxiety, and had no bad consequences for the cats' ability to carry out purposeful activities. Chlordiazepoxide and oxazepam were less effective in eliminating the neurotic symptoms. 11 references. (Journal abstract modified)

002513 Van Loon, Glen R.; Kim, Chul. Dept. of Medicine, Clinical Science Division, University of Toronto, Toronto, Canada M5S 1A8 **Dopaminergic mediation of beta-endorphin-induced catalepsy.** Research Communications in Chemical Pathology and Pharmacology. 21(1):37-44, 1978.

The interaction between subcataleptic doses of a neuroleptic and beta-endorphin in producing catalepsy was investigated in Sprague-Dawley rats. Acute intracisternal administration of human beta-endorphin produced catalepsy and increased striatal concentrations of 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA). All of these effects were blocked by naloxone. Apomorphine, a dopmine receptor antagonist, also prevented beta-endorphin-induced catalepsy and the increases in striatal DOPAC and HVA. The combination of subcataleptic doses of haloperidol and beta-endorphin produced catalepsy and large increases in striatal DOPAC and HVA. Data provide evidence for a role for nigrostriatal dopamine neurons in beta-endorphin-induced catalepsy. The apparent increase in striatal dopamine turnover following beta-endorphin administration may be compensatory. 21 references. (Author abstract modified)

002514 van Rossum, J. M. Department of Pharmacology, University of Nijmegen, Geert Grooteplein N 21, Nijmegen, The Netherlands **Two types of dopamine receptors in behavioral regulation.** Federation Proceedings. 37(10):2415-2421, 1978.

At the Annual Fall Meeting of the American Society for Pharmacology and Experimental Therapeutics held in Columbus, August 23, 1977, a paper was presented in which experimental proofs and arguments are advanced that two types of dopamine brain receptors (excitation-mediating and inhibition-mediating) exist. Modification of psychomotor stimulant action in rats and dopamine-haloperidol antagonism in the caudate nucleus of cats are described. The snail brain as a model of dopamine receptors is examined. The functioning of excitation-mediating and inhibition-mediating receptors in locomotor activity and stereotyped behavior is discussed along with the implications of dopaminergic involvement in a gratification system. 43 references. (Author abstract modified)

002515 Wakeley, Harold Glenn. Illinois Institute of Technology **Effects of cocaine on aggressive behavior. (Ph.D. dissertation.)** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 7800888, HC$15. MF$7.50. 85 p. 1977.

Models of affective and predatory aggression were used to determine the effectiveness of cocaine as an agent for modifying the expression of aggression. Thirty two pairs of male rats were trained to stable levels of foot shock elicited fighting behavior. Drug tests with isotonic saline, 8, 16, and 32mg/kg cocaine intraperitoneally yielded significant increases in fighting at all doses. Thirty experienced mouse killing rats, individually housed, were treated with isotonic saline, 8, 16, 32, or 64mg/kg cocaine. Killing behavior during a 5 minute period following mouse presentation was recorded for 10 days. All drug doses significantly inhibited mouse killing. A discussion of biogenic amine relationships to the expression of aggressive behavior is included. (Journal abstract)

002516 Walbran, Bonnie B.; Robins, Eli. Department of Psychiatry, Washington University Medical School, St. Louis, MO 63110 **Effects of central nervous system accumulation of tellurium on behavior in rats.** Pharmacology Biochemistry and Behavior. 9(3):297-300, 1978.

To study the effects of CNS accumulation of tellurium on rat behavior, 23 Ss were treated for 112 days with daily injections of 2mg/kg potassium tellurite in Sorensen's phosphate buffer or with the buffer vehicle only. At sacrifice, the cerbral gray matter of the Ss treated with tellurite was grossly darkened. The presence of tellurium in cerebellum was confirmed by atomic absorption spectrophotometry. Growth of the tellurite treated Ss was significantly impaired when compared with control Ss. However, in a T-maze, the activity level of the tellurite treated Ss was increased. On a simple delayed response task, the performance of the tellurite treated Ss was more consistent than that of the buffer treated Ss. 16 references. (Author abstract modified)

002517 Walker, William Alfred. Rutgers University, Newark **Hormonal induction of lordosis in female guinea pigs: behavioral and neurochemical correlates of estrogen action. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 7818120, HC$15. MF$7.50. 114 p. 1978.

A series of behavioral and neurochemical studies into the hormonal induction of lordosis in the female guinea-pig were undertaken. It was found that estrogen accumulation in the hypothalamic preoptic area (H-POA) neuronal nuclei reached a peak by 11 hours following subcutaneous injection of estradiol benzoate and remained at peak for 43 hours. Studies with the antiestrogens enclomiphene and CI-628 suggested that the induction of lordosis is dependent on the presence of estrogen in H-POA nuclei. Administration of various antiestrogens during a 60 hour estradiol priming period indicate a dose dependent inhibition of lordosis when antiestrogens were injected at 40 to 47 hours following estradiol injection. Injection of estradiol late in the priming period enhanced display of lordosis. A correlation between behavioral antiestrogenicity and in vitro competition for H-POA estrogen receptors was observed for all antiestrogens except MER-25. Relative binding affinities of antiestrogens compared to E2 suggested that the presence of estrogen in H-POA neurons just prior to and/or during the time of progesterone action is necessary for the optimum display of lordosis. Additional studies of various estrogens and antiestrogens are also presented. (Journal abstract modified)

002518 Walton, Nancy Y.; Deutsch, J. A. Dept. of Psychology, C-009, University of California, San Diego, La Jolla, CA 92093 **Self-administration of diazepam by the rat.** Behavioral Biology. 24(4):533-538, 1978.

To determine if rats can be induced to self-administer diazepam, male Charles River rats were offered the drug either orally or by counterinjection over a 6 day period, with concentrations increasing every other day. Although diazepam intoxication was observed at all drug concentrations and with increasing severity as the drug concentration was increased, no decrease in intake ensued. This apparent lack of conditioned aversion formation was not due to diazepam-induced amnesia, since rats poisoned with lithium chloride after diazepam consumption showed no attenuation of conditioned aversion when compared to rats poisoned after drinking flavored water. 15 references. (Author abstract modified)

002519 Watanabe, Hiroshi; Watanabe, Kazuo; Hagino, Koji. Department of Pharmacometrics, Research Institute for Wakanyaku, Toyama University, Toyama 930, Japan **The involvement of catecholamine in scopolamine-induced locomotor activation and rotational behaviour in mice.** Japanese Journal of Pharmacology (Kyoto). 28(3):465-472, 1978.

Scopolamine-induced locomotor activation was studied in comparison with the responses to apomorphine and methamphetamine in mice. Pretreatment with alpha-methyl-p-tyrosine, p-chlorophenylalanine, phenoxybenzamine, propranolol, haloperidol and pimozide was examined. The reduction of responses to the three agonists by pimozide and particularly by haloperidol suggest the involvement of catecholamine in the locomotor activation produced by scopolamine. Effects of the three agonists on a rotational behavior model which is sensitive to dopamine receptor stimulating agents were studied. Results indicate the participation of dopamine in the scopolamine-induced rotational behavior in mice. 26 references. (Author abstract modified)

002520 Wauquier, A. Dept. of Pharmacology, Janssen Pharmaceutica, B-2340 Beerse, Belgium **Differential action of dopamine agonists on brain self-stimulation behaviour in rats.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 236(2):325-328, 1978.

The effect of apomorphine on lever-pressing by rats for brain stimulation was compared with that of other dopamine (DA) agonists which have been shown to produce differential effects following intracerebral injections. It was expected that all would decrease high self-stimulation and that DA agonists at doses enhancing locomotor activity would increase low self-stimulation. It was found that five putative DA agonists behaved equally on high baseline self-stimulation, but differently on low baseline self-stimulation. It is suggested that an enhancement of locomotor activity may be related to the response enhancing effects of some DA agonists on low baseline self-stimulation and that the response increasing effects of certain DA agonists occur independently of their possible reinforcing properties. 5 references.

002521 Weibel, Stuart L.; Wolf, Harold H. University of Utah, Colege of Pharmacy, Salt Lake City, UT 84112 **Opiate modification of intracranial self-stimulation in the rat.** Pharmacology Biochemistry and Behavior. 10(1):71-78, 1979.

Studies were conducted in male Sprague-Dawley rats to confirm the involvement of central opiate receptors in the expression of opiate modulation of intracranial self-stimulation (ICSS). Biphasic, dose related changes in ICSS responding were observed following administration of morphine sulfate (1-25mg/kg ip) or levorphanol tartrate (LEV; 0.5-5mg/kg ip or 0.01-0.2mcmoles intraventricularly. Dextrophan did not elicit comparable effects after ip or intraventricular administration. The facilitatory and depressant phases of the LEV effect were both antagonized by naltrexone (10mcg, intraventricularly), which had no appraent effect on ICSS by itself. During a 5 day course of treatment, complete tolerance developed to the suppression of responding by 25mg/kg ip LEV, but not to the facilitatory effect of 0.5mg/kg ip LEV. The implications of these results for opiate reinforcement theory are considered. 44 references. (Author abstract modified)

002522 Whalen, Richard E.; Olsen, Kathie L. Dept. of Psychobiology, School of Biological Sciences, University of California, Irvine, CA 92717 **Prednisolone modifies estrogen-induced sexual differentiation.** Behavioral Biology. 24(4):549-553, 1978.

The aromatization hypothesis, which holds that androgens defeminize the brain only following their conversion to estrogens was tested in neonatal female rats. Ss were administered a low dose of estrogen alone or in combination with the glucocorticoid prednisolone a steroid that reduces blood levels of the estrogen binding protein. The estrogen significantly inhibited adult lordotic behavior only when combined with the prednisolone, a treatment which had no effect by itself. The findings support the hypothesis, as well as the suggestion that the fetoneonatal estrogen binding protein protects the developing rat from differentiating effects of estrogen. 16 references. (Author abstract modified)

002523 White, F. J.; Appel, J. B.; Kuhn, D. M. Behavioral Pharmacology Laboratory, Dept. of Psychology, Columbia, SC 29208 **Discriminative stimulus properties of quipazine: direct serotonergic mediation.** Neuropharmacology (Oxford). 18(2):143-151, 1979.

In male Sprague-Dawley rats trained to discriminate quipazine (1.0mg/kg ip) from saline in a two lever drug discrimination task, the 5-hydroxytryptamine (5-HT) precursor L-tyryptophan and the 5-HT reuptake blockers fluoxetine and citalopram failed to elicit responding on the quipazine appropriate lever. However, fenfluramine, which releases endogenous 5-HT from nerve terminals, produced 84% quipazine appropriate responding. The dopamine agonists apomorphine and amphetamine did not transfer to quipazine. Para-chlorophenylalanine, which depletes central 5-HT by inhibiting its synthesis, significantly potentiated a subthreshold dose (0.25mg/kg) of quipazine and reduced the transfer of fenfluramine to quipazine, suggesting that quipazine exerts its discriminatory effect by directly stimulating central 5-HT receptors. Mescaline, d-lysergic acid diethylamide, and psilocybin all produced strong transfers to the quipazine cue, suggesting the possibility that quipazine may posses hallucinogenic properties. 47 references. (Author abstract modified)

002524 White, Norman; Brown, Zavie; Yachnin, Michael. Department of Psychology, McGill University, 1205 McGregor Ave., Montreal, Quebec, H3A 1B1, Canada **Effects of catecholamine manipulations on three different self-stimulation behaviors.** Pharmacology Biochemistry and Behavior. 9(3):273-278, 1978.

Rats with self-stimulation electrodes in the medial part of the lateral hypothalamus (LH) or in the lateral part of LH were trained to bar press, to run in a continuous square=shaped runway, and to move their tails from side to side while otherwise restained, all using LH stimulation on an FI 2 sec reinforcement schedule. At low doses of pimozide (a dopaminergic blocker) or of FLA-57 (a dopamine beta-hydroxylase inhibitor) different effects of responding rates were observed on each of the three tasks at the two electrode placements, indicating that the reductions were not due to the specific performance effects of the drugs. Rate change patterns suggest that the effects of LH stimulation on runway behavior are primarily, but not ex-

clusively, mediated by a dopaminergic system; that the effects of LH stimulation on tail movement are primarily, but not exclusively, mediated by a noradrenergic system; and that the effects on bar pressing are mediated by both, or either, of these substrates. Results suggest that the reinforcement of behavior by LH stimulation is flexibly mediated by at least two different neural systems. 36 references. (Author abstract)

002525 Williams, C. H.; Dollie, F. Dept. of Mental Health, Queen's University, Belfast, N. Ireland **Biochemical and behavioural studies of monoamine oxidase inhibition.** Irish Journal of Medical Science (Dublin). 147(Supplement 1):71-74, 1978.

A paper read at the first Irish Psychopharmacology Conference, held in Belfast in March 1978, is presented. The effects of d1-N-propargyl amphetamine on monoamine oxidase in rat brain were studied. It was found that injection of this compound produced a marked stereotyped response. It was also found to potentiate the stereotypy produced by amphetamine. Subsequent examination of monoamine oxidase activity in the brains of the animals showed substantial inhibition of the B form of this enzyme but no effect on the A form. The optical isomers of N-propargyl amphetamine were prepared and their inhibitory activity in vitro against monoamine oxidase in rat liver mitochondria was assessed. The l-isomer was found to be a better inhibitor than the d-isomer. 9 references. (Author abstract modified)

002526 Willmore, L. James; Sypert, George W.; Munson, John B. Neurology Service (127), Veterans Administration Hospital, Gainesville, FL 32602 **Recurrent seizures induced by cortical iron injection: a model of posttraumatic epilepsy.** Annals of Neurology. 4(4):329-336, 1978.

An experimental model of human focal epilepsy was demonstrated which has the potential of reflecting the pathogenetic mechanisms responsible for the posttraumatic epilepsies in man. A single injection of ferrous or ferric chloride into rat or cat sensorimotor cortex resulted in chronic recurrent focal paroxysmal electroencephalographic discharges as well as behavioral convulsions and electrical seizures. Iron filled macrophages, ferruginated neurons, and astroglial cells surrounded the focus of seizure discharge. It is suggested that the development of human posttraumatic epilepsy may depend, in part, on neurochemical alterations induced by the principal metallic ions found in whole blood. 37 references. (Author abstract modified)

002527 Winter, J. C. School of Medicine, State University of New York at Buffalo, Buffalo, NY 14214 **Drug-induced stimulus control.** In: Blackman, D., Contemporary research in behavioral pharmacology. New York, Plenum, 1978. 506 p. (p. 209-237).

Selected aspects of drug-induced stimulus control are examined by exploring the experimental methods and by interpreting data generated by the methods. Topics discussed include: a definition of terminology, response choice, T-maze, two lever choice, response emission, approach/avoidance, response rate, compound stimuli, dose-effect relationships, cross tests, origin and nature of drug-induced stimuli, and sensory pathways. 60 references.

002528 Winter, J. C. Dept. of Pharmacology and Therapeutics, School of Medicine, State University of New York, Buffalo, NY 14214 **Yohimbine-induced stimulus control in the rat.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 235(1):86-92, 1978.

Six female CFN rats were trained to discriminate yohimbine hydrochloride (3mg/kg i.p.)from saline. The rats achieved criterion performance (80% correct responses in each of five consecutive sessions) after a mean of 33 sessions. When the yohimbine trained rats were cross-tested with d-amphetamine, harmaline, and lysergic acid diethylamide, each test drug elicited responding intermediate to that induced by yohimbine and saline. No significant antagonism of yohimbine-induced stimulus control was achieved with BC-105, phentolamine, or butaclamol, which are believed to be antagonists at serotonergic, alpha-adrenergic, and dopaminergic receptor sites, respectively. 24 references. (Author abstract modified)

002529 Wojcik, Magdalena; Niemierko, Stella. Nencki Institute of Experimental Biology, Pasteura 3, 02-093 Warsaw, Poland **The effect of synthetic scothophobin on motor activity in mice.** Acta Neurobiologiae Experimentalis (Warszawa). 38(1):25-30, 1978.

The motor activity of mice treated by scotophobin (1, 2, 4, 6mcg) was tested in a photoresistor actometer 24, 48 and 72 hours after injection. Scotophobin in doses of 4 and 6mcg per mouse significantly increased motor activity as compared with controls injected with saline only. The result suggests that shortening of dark box time, found by some investigators after injection of scotophobin, seems to be the consequence of the enhanced motor activity of mice. It is concluded that the effect of scotophobin on the behavior of animals is not specific and that this substance cannot be considered responsible for memory transfer. 13 references. (Author abstract)

002530 Woolverton, W. L.; Kandel, David; Schuster, Charles R. Department of Pharmacology, Medical College of Virginia, Richmond, Va 23298 **Effects of repeated administration of cocaine on schedule-controlled behavior of rats.** Pharmacology Biochemistry and Behavior. 9(3):327-337, 1978.

The effects of cocaine (4.0to 32mg/kg) on schedule controlled behavior of rats were determined before and during a period of repeated administration of cocaine. In rats trained to lever press on a fixed ratio 40 schedule for food delivery, 8.0to 32mg/kg cocaine initially decreased response rate in a dose related manner. During repeated administration, cocaine effects on response and running rates were attenuated in two Ss and did not change in two others. When dose effect functions were redetermined, a shift to the right was observed in several measures, indicating the development of tolerance. In rats trained to lever press on a DRL 20" schedule for food delivery, cocaine (4.0to 32mg/kg) increased response rates, decreased number of reinforcements per session, and shifted interresponse time distributions to the left. During repeated administration, the effects of the daily dose (16mg/kg) on all measures were attenuated. Tolerance was further indicated by a shift in the dose effect function of cocaine to the right during the redetermination. 34 references. (Author abstract modified)

002531 Yaksh, Tony L. Mayo Clinic and Foundation, Rochester, MN 55901 **Analgetic actions of intrathecal opiates in cat and primate.** Brain Research (Amsterdam). 153(1):205-210, 1978.

In a study of the analgetic actions of intrathecal opiates in cats and Rhesus monkeys, behaviorally defined analgesia was produced by a pharmacologically specific action of intrathecally administered morphine or methadone. Results suggest that the profoundly elevated nociceptive thresholds produced by intrathecal action of opiates do not appear to be associated with alterations in coordinated motor functions or the basic vegetative patterns of the animal, such as respiration, heartrate, or urination. The presence of opiate binding in the substantia gelatinosa, along with the known modulatory capacity of this region, suggest that this region is a likely site of the analgesic action. The clinical relevance of the procedure for the relief of chronic pain in cancer patients is noted. 20 references.

002532 Yoshimura, Hidetoshi; Watanabe, Kazuhito; Oguri, Kazuta; Fujiwara, Michihiro; Ueki, Showa. Faculty of Pharma-

ceutical Sciences, Kyushu University, Fukuoka 812, Japan **Synthesis and pharmacological activity of a phosphate ester of delta8-tetrahydrocannabinol.** Journal of Medicinal Chemistry. 21(10):1079-1081, 1978.

A water soluble phosphate ester of delta8-tetrahydrocannabinal (delta8-THC) was synthesized and its pharmacological activity was examined in the mouse. The cataleptogenic and thiopental sleep potentiating effects of delta8-THC phosphate in the mouse were approximately 10% and 7% of those of delta8-THC, respectively. However, this phosphate showed almost the same potency and a longer duration of hypothermic effect, as compred with delta8-THC. The acute toxicity of delta8-THC phosphate was far lower than that of delta8-THC. Delta8-THC phosphate was difficulty hydrolyzed by alkaline phosphatase or mouse liver homogenate in vitro. The model of action of this phosphate derivative is discussed in connection with this enyzmatically difficult hydrolysis. 9 references. (Author abstract)

002533 Yutrzenka, G. J.; Parmar, S. S.; Davis, J. S. Department of Physiology, University of North Dakota School of Medicine, Grand Forks, ND 58202 **Mediation by catecholamines of the anticonvulsant activity of diazepam.** Research Communications in Psychology, Psychiatry and Behavior. 4(1):79-88, 1979.

The role of central catecholamines as mediators of the anticonvulsant activity of diazepam was investigated. Diazepam, administered in doses of 1mg/kg and 2mg/kg provided protection against pentylenetetrazol-induced convulsions in male albino mice. Pretreatment with either reserpine, alpha-methyl-p-tyrosine, L-dopa, phenoxybenzamine, or propanolol, prior to diazepam administration, potentiated the observed anticonvulsant activity of diazepam. However, pretreatment with disulfiram produced essentially no change in the anticonvulsant activity of diazepam. These results provide evidence for the possible role of adrenergic pathways in the anticonvulsant activity of diazepam. 33 references. (Author abstract)

002534 Zvartau, E. E.; Patkina, N. A. Kafedra farmakologii 1-go meditsinskogo instituta im. I. P. Pavlova, Leningrad, USSR / **Change of hypothalamic electrical stimulation escape response in rats under chronic morphine administration./** Izmeneniye reaktsii vyklyucheniya elektricheskoy stimulyatsii gipotalamusa u krys pri khronicheskom vvedenii morfina. Zhurnal Vysshey Nervnoy Deyatel'nosti imeni I. P. Pavlova (Moskva). 28(5):1020-1026, 1978.

Nine male rats (weight 200 to 350g) with electrodes implanted in the hypothalamus were trained to exhibit a conditioned response to electrical stimulation. The rats, placed in one section of their cage to receive the shock, could cut off the electrical current by moving into another section. After acquiring this reflex, the rats were given 12 to 30 injections of morphine in increasing doses: from 20 up to 180mg/kg per injection. The drug was found to have a dose proportional suppressive effect on the reflex. In the course of repeated injections, an absolute or relative tolerance to the suppressive effect developed in the responses, both to central and to peripheral pain stimulation. The suppressive action was judged to be specific and not correlated with the rats' catatonic reaction or to changes of general motor activity. A gnawing response was activated after injections of 60mg/kg and higher. The suppression of reactions to adverse stimuli was judged to be an important element in the development of morphine addiction. 10 references. (Journal abstract modified)

05 TOXICOLOGY AND SIDE EFFECTS

002535 Bhargava, Hemendra N. Dept. of Pharmacognosy and Pharmacology, College of Pharmacy, University of Illinois at the Medical Center, Chicago, IL 60612 **Quantitation of morphine tolerance induced by pellet implantation in the rat.** Journal of Pharmacy and Pharmacology (London). 30(2):133-135, 1978.

The degree of morphine tolerance produced in the rat by five different schedules of subcutaneous morphine implantation was investigated. The schedules differed in the number of pellets used and the interval between implantations. Rats in schedules 2 to 4 developed 6, 8 and 13 fold tolerance to morphine, respectively. It was found that implantation of two morphine pellets produces a low degree of tolerance. The rats that were less tolerant to morphine had lower brain and plasma concentrations of morphine as well as faster rates of disappearance of the drug from brain and plasma compared with the more tolerant rats. It is suggested that caution be exercized when comparing interspecies data concerning the biochemical mechanisms of morphine intolerance and that the degree of tolerance should be assessed quantitatively before such comparisons are made. 14 references.

002536 Bracy, Odie L.; Doyle, Rebecca S.; Kennedy, Maurice; McNally, Stephen M.; Weed, J. Duane; Thorne, B. Michael. Mississippi State University, Mississippi State, MS 39762 **Effects of methomyl and ethanol on behavior in the Sprague-Dawley rat.** Pharmacology Biochemistry and Behavior. 10(1):21-25, 1979.

The emotional behavior and activity levels of male Sprague-Dawley rats were studied following administration of ethanol and/or methomyl, a carbamate pesticide, in a ground chow diet. The experimental diets resulted in reduced acetylcholinesterase (AChE) levels. The greatest AChE reduction was seen in the methomyl group, which also showed the least evidence for habituation in an open field test. The treated animals did not differ from controls on handling and muricide tests. 22 references. (Author abstract modified)

002537 Bushnell, Philip J. University of Wisconsin, Madison **Behavioral toxicology of lead in the infant rhesus monkey. (Ph.D. dissertation).** Dissertation Abstracts International. 39(5):2560-B, 1978. Ann Arbor, Univ. Microfilms No. 7815037, 162p., 1978.

A primate model of the behavioral toxicology of chronic, low level lead exposure was explored, where in each of three separate experiments, infant rhesus monkeys were fed lead acetate daily in milk formula for the first year of life. Blood lead concentrations (BLCs) were maintained by dose adjustments in separate experimental groups in low or high chronic ranges, or were elevated to a transient peak level during weeks 5 and 6 postpartum. Control animals in each experiment received identical diets without added lead. Spontaneous activity, learning, capacity, and social development were evaluated for all animals during and after lead dosing period. Results from Experiment 1 show that animals at both exposure levels are hyperactive at 18 months of age, but are normal or hypoactive where observed in the home cage and in social groups. Lead-induced hyperactivity is not shown in experiments 2 or 3. In all experiments, animals with high BLCs are extremely retarded in learning the first of a series of reversals in a reversal learning set paradigm, despite normal acquisition of the discrimination and performance of subsequent reversals in the series. Chronic exposure to lead impairs social development in a dose related manner, as is evidenced by significant suppression of interactive play and assertive behaviors in all experiments, and by significant increases in social clinging responses in Experiments 1 and 2. Results are discussed in terms of critical organ and concentration concepts for lead toxicity, and the possibility that behavioral response to chronic lead exposure in animals may mimic the effects of damage to the hippocampus. (Journal abstract modified)

002538 Clement, J. G. Defence Research Establishment Suffield, Biomedical Section, Ralston, Alberta, Canada **Effect of**

ethanol, pentobarbital and morphine on the toxicity of hemicholinium-3 and d-tubocurarine in mice. Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 236(1):60-65, 1978.

The effects of ethanol, pentobarbital, and morphine on the toxicity of hemicholinium-3 and d-tubocurarine in mice were examined. The pretreatment of mice with either ethanol, pentobarbital, or morphine protected against the lethal effects of hemicholinium-3 (HC-3) but not curare. The protective action of these compounds was not due to an induced release of corticosteroids in vivo since administration of prednisolone did not protect against HC-3 toxicity. It is concluded that the site of the protective action of ethanol, pentobarbital, and morphine and the site of action of the lethal respiratory depression by HC-3 are central in origin. 13 references. (Author abstract modified)

002539 Earley, C. J.; Leonard, B. E. Department of Pharmacology, University College, Galway, Ireland **Androgenic involvement in conditioned taste aversion.** Hormones and Behavior. 11(1):1-11, 1978.

The effects of castration and hormone substitution on conditioned taste aversion behavior were investigated in male rats. Conditioning involved the pairing of a novel solution (sucrose) with toxicity induced by lithium chloride. Two days later, conditioned animals showed an aversion to sucrose solution, although consumption of water was not affected. Differences in treatment groups emerged during the subsequent extinction period. Within 15 days virtually all of the castrated control animals had a greater than 50% preference for sucrose, while sham operated animals retained their initial aversion to the solution. Treatment with testosterone or dihydrotestosterone was effective in maintaining a conditicned response to sucrose that was compatible with sham animals. An estrogen precursor, 19-hyrdoxytestosterone, was ineffective in altering the castration effect. The androgenic properties of this behavior were further clarified when cyproterone acetate was found to block the effects of testosterone on this behavior. The results implicate the involvement of androgens in the extinction of a conditioned taste aversion. 27 references. (Author abstract modified)

002540 Hedlund, Britta; Gamarra, Marilena; Bartfai, Tamas. Dept. of Biochemistry, Arrhenius Laboratory, University of Stockholm, S-106 91 Stockholm, Sweden **Inhibition of striatal muscarinic receptors in vivo by cadmium.** Brain Research (Amsterdam). 168(1):216-218, 1979.

The effects of chronic exposure to cadmium (Cd2) in vivo on muscarinic receptors in the brain were examined in male Sprague-Dawley rats. Specific (3H)3-quinuclidinyl benzilate binding was significantly reduced in the striatum and cerebral cortex of rats exposed to 1 or 10mM Cd2 for 8 days; the muscarinic binding sites in the striatum were reduced by 50%. Addition of the chelating agent ethylenediaminetetraacetate (1mM) together the Cd2 (lmM) in the drinking water reduced the loss of striatal muscarinic receptors to 20-25%. Muscarinic receptors were also inhibited by about 50% by exposure to 100mcm Cd2 in vitro. 12 references.

002541 Holtzman, D.; Hsu, J. Shen; Mortell, P. Dept. of Neurology, Stanford University School of Medicine, Stanford, CA 94305 **In vitro effects of inorganic lead on isolated rat brain mitochondrial respiration.** Neurochemical Research. 3(2):195-206, 1978.

The effects of lead acetate on respiration in cerebral and cerebellar mitochondria from immature and adult Sprague-Dawley rats were studied polarographically. With all substrates, low lead concentrations produced an increase in respiration. Higher concentrations inhibited both lead-induced respiration and adenosine diphosphate dependent respiration. Lead-induced respiration required inorganic phosphate and was inhibited by oligomycin, suggesting coupling to oxidative phosphorylation. Inhibition of respiration was produced by much lower lead concentrations with nicotinamide adenine dinucleotide (NAD) linked citric acid cycle substrates than with succinate or alpha-glycerophosphate. In partially disrupted mitochondria, NAD linked substrate oxidation was inhibited at lead concentrations than did not affect NADH oxidation. Thus, in brain mitochondria the NAD linked dehydrogenases, located in the matrix space, were more sensitive to inhibition by lead than were inner membrane enzymes. All in vitro lead effects on mitochondrial respiration were comparable in cerebral and cerebellar mitochondria isolated from both immature and adult rats. 30 references. (Author abstract)

002542 Mohrland, J. Scott; Craigmill, A. L. Dept. of Pharmacology, University of Iowa College of Medicine, Iowa City, IA 52242 **The effect of aggregation on the lethality of morphine in mice.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 236(2):252-265, 1978.

Certain factors previously found to be involved in amphetamine aggregate toxicity were studied in relation to aggregation enhancement of morphine toxicity. Morphine was found to be more lethal to mice housed in groups than to mice housed individually. The aggregation effect on morphine lethality was increased when ambient temperature was increased to 29 degrees C and abolished when ambient temperature was lowered to 19 degrees C. At 29 degrees C morphine produced hypothermia and lower locomotor activity in isolated mice and hyperthermia and higher locomotor activity in aggregated mice; at 19 degrees C all morphine treated mice were hypothermic and there was no significant difference in locomotor activity. The locomotor activity time course of morphine treated aggregated mice at 29 degrees C closely resembled the rectal temperature time course, suggesting that the hyperthermia involved an increase in heat production via an increase in locomotor activity. However, the hyperthermia observed was not sufficient to explain the increased lethality in aggregated mice. Differences between aggregation effect on morphine lethality and that previously reported for amphetamine are discussed. 24 references. (Author abstract modified)

002543 Montalcini-Levi, Rita. Washington University, St. Louis, MO 63130 **Toxicity of psychotropic drugs on aminergic neurons.** Final Report, NIMH Grant, R01-MH-24604, 1978. 10 p.

Four experiments investigated the toxicity of psychotropic drugs on aminergic neurons in mammalian and amphibian tissue. In Experiment 1, radioimmunoassay was used to determine nerve growth factor (NGF) content in tissues, organs, and organic fluids in mammalian and amphibian tissue. Experiment 2 performed autoradiographic tracing of intracerebral neuronal circuits in rat brain. Retrograde horseradish tracing method was also used. In Experiemnt 3, the localization of the two brain specific proteins S-100 and 14-3-2 in neurons, glia, and other satellite cells was studied via immunofluorescence in brains of avian embryos and rat fetuses. Experiment 4 purified choline acetyle transferase (CAT) from beef caudate nucleus using ammonium sulfate fractionation, gel filtration, ion exchange chromatography, and affinity chromatography. Methodological problems are described, as well as the marked methodological improvements achieved in Experiment 4. Future research will investigate the effects of antiserum on the NGF and the destructive effects produced by 6-OHDA in the immature adrenergic neuron. 15 references.

002544 Musch, H. R.; Bornhausen, M.; Kriegel, H.; Greim, H. Department of Toxicology, Gesellschaft fur Strahlen- und Um-

weltforschung mbH, D-8042 Neuherberg, Germany **Methylmercury-chloride-induced learning deficits in prenatally-treated rats.** Archives of Toxicology (Berlin). 40(2):103-108, 1978.

The effects of prenatal exposure to methylmercury chloride (MMC) on learning were examined in Wistar rats. MMC was given to pregnant rats on days 6-9 after conception in doses of 0.05 or 2.0mg/kg/day. The female offspring of these animals were tested 90 days after birth for learning ability in a food reward, bar-press paradigm. The MMC treated rats showed significant deficiencies in acquisition speed when the ratio of barpresses to reward was increased in a classical contingency of differential reinforcement of high rates. No differences in general motility or motor coordination were observed. 19 references. (Author abstract modified)

002545 Rafales, Lee S.; Bornschein, Robert L.; Michaelson, I. Arthur; Loch, Rita K.; Barker, Greg F. Department of Environmental Health, University of Cincinnati, College of Medicine, Cincinnati, OH 45267 **Drug-induced activity in lead-exposed mice.** Pharmacology Biochemistry and Behavior. 10(1):95-104, 1979.

Locomotor activity was examined in CD-1 mice exposed to lead via maternal milk prior to weaning or via the water supply after weaning. The spontaneous activity of lead exposed and control mice did not differ significantly. However, locomotor activity in response to challenge doses of d-amphetamine, methylphenidate, apomorphine, or phenobarbital varied in a complex manner as a function of the magnitiude and duration of lead exposure. Depressed body weight concurrent with high lead exposure also had significant effects on both spontaneous and drug-induced activity. 26 references. (Author abstract modified)

002546 Savolainen, H.; Pfaffli, P.; Helojoki, M.; Tengen, M. Dept. of Industrial Hygiene and Toxicology, Institute of Occupational Health, Haartmaninkatu 1, SF-00290 Helsinki 29, Finland **Neurochemical and behavioural effects of long-term intermittentt inhalation of xylene vapour and simultaneous ethanol intake.** Acta Pharmacologica et Toxicologica (Kobenhavn). 44(3):200-207, 1979.

The neurochemical and behavioral effects of long-term inhalation of xylene vapor and simultaneous ethanol intake were investigated in male Wistar rats. Intermittent exposure of 2-month-old rats to 300ppm xylene vapor for 5 to 18 weeks resulted in increased microsomal superoxide dismutase activity in the brain. Concomitant ethanol ingestion added significantly to the xylene effects by causing increased proteolysis during weeks 9 and 14; cerebral superoxide dismutase did not increase in these animals, however. Preening frequency decrased transiently in ethanol and in xylene treated groups at 6 and 9 to 12 weeks, respectively. Increased ambulation was observed only in the xylene/ethanol combined treatment group, after 12 and 14 weeks of exposure. These findings suggest a significant interaction between the two solvents. 46 references. (Author abstract modified)

002547 Sharma, K. K.; Sen, P.; Bapna, J. S.; Khanna, T. Dept. of Pharmacology and Therapeutics, University College of Medical Sciences, Ring Rd., New Delhi 110016, India **Potentiation of anticonvulsant effects of diphenylhydantoin by sulfonamides in the rat.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 236(2):266-275, 1978.

The effect of single or repeated doses of some antibacterial sulfonamides on the antiseizure activity of diphenylhydantoin (DPH) was studied in rats. It was found that in animals pretreated with sulfonamides the subeffective dose of DPH produced a significant antiseizure activity. The possibility of displacement of DPH by sulfonamides from its protein binding site was explored, and the serum level of DPH was shown to be significantly less in animals pretreated with sulfonamides, indicating that these drugs displaced DPH to make it available at biophase in high concentration. It was inferred that a measurement of serum concentration of DPH in such a situation may not be as indicative of magnitude of effect or drug concentration at biophase as it is in subjects treated with DPH alone. It is suggested that the DPH spared from the protein binding was responsible for the enhancement of its action, and that the simultaneous use of two drugs may lead to serious DPH toxicity. 18 references. (Author abstract modified)

002548 Smith, Donald F. Psychopharmacology Research Unit, Psychiatric Hospital, Risskov, Denmark **Lithium chloride toxicity and pharmacodynamics in inbred mice.** Acta Pharmacologica et Toxicologica (Kobenhavn). 43(1):51-54, 1978.

Inbred strains of male mice (C3H, DBA, BALB, C57) were used to determine whether genetic factors play a role in lithium toxicity. Significant differences in the LD50 for lithium chloride (LiCl) were observed between the mouse strains after a subcutaneous injection of 37 isotonic LiCl. The LD50 values in the C3H, DBA, BALB and C57 strains were 17.4, 17.6, 18.2, and 19.4mmol/kg, respectively. Significant differences were also observed between the mouse strains in the concentrations of lithium in plasma, heart, liver, kidney, and brain, 2 hours after a subcutaneous injection of 15.1or 18.2mmol/kg LiCl, but the lithium concentrations were not related in an obvious manner to LiCl toxicity. 11 references. (Author abstract modified)

002549 Sobotka, T. J.; Brodie, R. E.; Spaid, S. L. Division of Toxicology, Food and Drug Administration, Washington, DC 20204 **Neurobehavioral studies of tremorgenic mycotoxins verruculogen and penitrem A.** Pharmacology (Basel). 16(5):287-294, 1978.

The behavioral and neurochemical effects of verruculogen (V) and penitrem-A (PA), two toxic secondary metabolites of mold contaminants of foodstuffs known as tremorgenic mycotixins, were examined. In mice, the median tremorgenic doses were 0.92mg/kg ip for V and 0.19mg/kg ip for PA. Both V and PA depressed spontaneous motor activity and exploratory reflex behaviors in mice; significant motor depression was observed even at doses that were not accompanied by any overt signs of neurotoxicity. Acquisition of a conditioned avoidance shuttle response was disrupted, but only by a high neurotoxic dose of V. Neurochemical analyses revealed no clear catecholaminergic or cholinergic involvement in the neurotoxic syndrome produced by V or PA. 18 references. (Author abstract modified)

002550 Wahlstrom, Goran; Nordberg, Agneta. Department of Pharmacology, University of Umea, S-901 87 Umea, Sweden **Decreased brain weights in rats after long-term barbital treatments.** Life Sciences (Oxford). 23(15):1583-1590, 1978.

Male Sprague-Dawley rats given a solution of barbital as their only drinking fluid for about 30 weeks and then withdrawn for various periods prior to sacrifice had consistently reduced wet brain weights compared to untreated controls. This reduction was not restituted after an abstinent period of 30 days. The decrease did not seem to be secondary to reduced bodyweight and was not influenced by changes in water intake during the abstinent period. A similar, smaller reduction was seen in rats treated with barbital for 12 weeks. Results are discussed in relation to the brain atrophy found in humans after long-term ethanol abuse. 14 references. (Author abstract modified)

06 METHODS DEVELOPMENT

002551 Aono, Junichiro; Takahashi, Masakatsu; Koida, Masao. Department of Pharmacology, Faculty of Pharmaceutical Sci-

ences, Nagasaki University, Nagasaki 852, Japan **An assay method of brain enzyme carving beta-endorphin into methionine enkephalin.** Japanese Journal of Pharmacology (Kyoto). 28(6):930-932, 1978.

An assay for the enzyme that breaks down beta-endorphin to form methionine enkephalin is described. The method involves a radioimmunoassay that is highly specific for methionine enkephalin, showing no interference from leucine enkephalin, beta-lipotropin, or endorphins. Preliminary evidence for the existence of the methionine enkephalin forming enzyme in brain is presented. 9 references.

002552 Ben-Ari, Y.; Tremblay, E.; Ottersen, O. P.; Naquet, R. Laboratoire de Physiologie nerveuse, Dept. de Neurophysiologie appliquee, CNRS, F-91190 Gif-sur-Yvette, France **Evidence suggesting secondary epileptogenic lesions after kainic acid: pretreatment with diazepam reduces distant but not local brain damage.** Brain Research (Amsterdam). 165(2):362-365, 1979.

Pretreatment with diazepam (20-30mg/kg ip) blocked the convulsive seizures and secondary hippocampal damage induced by intracerebroventricular injections of kainic acid (KA), without reducing the direct toxic action of KA at the site of injection. These results suggest that the distant brain lesions normally observed after KA injection may be secondary to the sustained epileptiform activity induced by KA. The systematic use of pretreatment with an anticonvulsant is recommended to limit distant brain damage in neurochemical studies in which KA is used as a tool to induce local lesions. 13 references.

002553 Berger, Brigitte. INSERM U134, Laboratoire de Neuropathologie Charles Foix, Hopital Salpetriere, F-75634 Paris, Cedex 13, France **In vitro uptake of dopamine in serotonergic nerve terminals: a fluorescence histochemical study on vibratome sections of the rat cerebral cortex.** Advances in Biochemical Psychopharmacology. 19:405-408, 1978.

An in vitro method for separate visualization of noradrenergic and dopaminergic nerve terminals in rat cerebral tissue sections was developed. Following pharmacological depletions of catecholamine stores, fluorescence histochemical studies were performed on thin tissue sections from normal or lesioned rats. The sections were incubated in the presence of different exogenous amines or catecholamine inhibitors, and the minimal concentrations of amines and drugs were determined. This method permitted visualization of serotonergic, as well as noradrenergic and dopaminergic, nerve terminals under various experimental conditions. The uptake of dopamine not only in catecholaminergic but also in serotonergic terminals was observed using this method. 11 references.

002554 Damm, Heinz W.; Muller, Walter E.; Schlafer, Uwe; Wollert, Uwe. Pharmakologisches Institut der Universitat Mainz, D-6500 Mainz, Germany **(3H) Flunitrazepam: its advantages as a ligand for the identification of benzodiazepine receptors in rat brain membranes.** Research Communications in Chemical Pathology and Pharmacology. 22(3):597-600, 1978.

The advantages of 3H flunitrazepam as a ligand for the identification of benzodiazepine receptors in rat brain membranes were compared with those of 3H diazepam. For the typical assay procedure, unspecific binding obtained with 3H flunitrazepam was three to four times less than unspecific binding obtained with 3H diazepam. Using 3H flunitrazepam for the centrifugation assay, the unspecific binding is as low as found for filtration assays. 9 references.

002555 Ebara, Takashi; Smith, Donald F. Dept. of Neuropsychiatry, Okayama Medical School, Okayama, Japan **A method to determine lithium content in blood platelets.** Acta Pharmacologica et Toxicologica (Kobenhavn). 44(3):238-240, 1979.

In a letter to the editor, a method for determining the lithium content of blood platelets which was developed and tested in male Wistar rats is described. Animals were given a stomach load of 0.15M lithium chloride (1, 1.5, or 2mmol/kg) twice daily for 4 days. Between 4 and 17 hours after the last dose of lithium, blood was drawn from the abdominal aorta into a glass syringe containing ethylenediaminoetetraacetate (EDTA). The blood/EDTA solution was centrifuged at 140xg for 12 minutes at 4 degrees. The platelet rich plasma product was passed through type-RA millipore filters, which were washed twice in cold isotonic magnesium chloride. Results indicate that the content of lithium in the platelets increased significantly with increases in the daily dose of lithium. Preliminary studies indicate that this method can also be used to determine the lithium content in human blood platelets. 10 references.

002556 Fadloun, Z.; Leach, G. D. H. Schools of studies in Pharmacology, University of Bradford, W. Yorks, England **Measurements of noradrenaline overflow and dopamine-beta-hydroxylase activity in superfused preparations.** British Journal of Pharmacology (London). 64(3):464P, 1978.

In a paper presented at the September 1978 meeting of the British Pharmacological Society at the University of Nottingham, a method for simultaneous measurement of noradrenaline (NA) concentration and dopamine-beta-hydroxylase (DBH) activity in superfused rat anococcygeus muscle and vas deferens preparations is described. The combination of superfusion method and perimural stimulation is achieved by attaching the tissue on a specially constructed perspex holder, with stimulation from two platinum electrodes. The gap between the electrodes and the tissue is made wide enough to allow the muscle to contract freely, but for the superfusate to be retained by capillary action, thus acting as medium for electrical stimulation. Phenoxybenzamine, yohimbine, phentolamine, and desmethylimipramine significantly increased both NA overflow and DBH activity in the superafusate after tissue stimulation in these preparations. 8 references. (Author abstract modified)

002557 Gulliver, Peter A.; Tipton, Keith F. Department of Pharmacology, Medical and Dental Building, The University, Leeds LS2 9JT, England **The purification and properties of pig brain catechol-0-methyltransferase.** Journal of Neurochemistry (Oxford). 32(5):1525-1529, 1979.

An affinity chromatography technique was adapted for the large scale purification of pig brain catechol-0-methyltransferase. The enzyme prepared by this method is apparently homogenous by polyacrylamide gel electrophoresis criteria and is stable for prolonged periods of storage at -5 degrees in 20% glycerol. Kinetic measurements, molecular weight criteria, and antiserum reaction suggest that the brain and liver forms of catechol-0-methyltransferase are closely related, if not identical. 22 references. (Author abstract modified)

002558 Hanin, Israel. Western Psychiatric Institute and Clinic, Dept. of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261 **Anesthetics and central cholinergic function -- a perspective.** Anesthesiology. 48(1):1-3, 1978.

Research development on central cholinergic function is sketched, and methodological problems in the study of the involvement of the central cholinergic system in anesthesia are reviewed. Methodological breakthroughs in central cholinergic function are discussed, including: introduction of novel techniques to kill experimental animals rapidly while inactivating endogenous enzymes within seconds; availability of dependable, sensitive, and specific methods for the analysis of levels and me-

tabolism of choline and its metabolites; and appropriate techniques with which to calculate the rate of turnover of brain acetylcholine in vivo. 38 references.

002559 Innis, Robert B.; Bylund, David B.; Snyder, Solomon H. Department of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **A simple, sensitive and specific radioreceptor assay for beta-adrenergic antagonist drugs.** Life Sciences (Oxford). 23(20):2031-2038, 1978.

A radioreceptor assay for beta-adrenergic blocking drugs is described. The assay is based on the ability of the blood content of drugs to compete with the binding of 3H-dihydroalprenolol (3H-DHA) to beta-adrenergic receptors in calf cerebellar membranes. Plasma protein greatly inhibits the binding of 3H-DHA to the beta receptors. As little as 0.01ml of human plasma in a final volume of 1ml reduces binding 25% to 45%. Assays conducted on plasma dialysates can be performed without such inhibition. The radioreceptor assay is simple to perform, and 100 samples can be processed in a morning. It is sensitive, detecting low nanomolar concentrations of plasma propranolol, and it is specific. No clinically employed drugs other than beta-blocking agents compete for beta-receptor bonding. The assay detects all pharmacologically active metabolites of beta-blocking drugs, as well as the parent drug. 13 references. (Author abstract modified)

002560 Lorden, Joan F.; Oltmans, Gary A.; Dawson, Ralph, Jr.; Callahan, Michael. Department of Psychology, University of Alabama, Birmingham, AL 35294 **Evaluation of the non-specific effects of catecholamine and serotonin neurotoxins by injection into the medial forebrain bundle of the rat.** Pharmacology Biochemistry and Behavior. 10(1):79-86, 1979.

Low doses of 6-hydroxydopamine (6-OHDA), 5,6-dihydroxytryptamine (5,6-DHT), and 5,7-dihydroxytryptamine (5,7-DHT) were injected into the female rat medial forebrain bundle, which contains serotonin (5-HT), norepinephrine (NE), and dopamine (DA) fibers. Damage to these fibers was quantified by measuring depletion of 5-HT, NE, and DA in the telencephalon, and the effects of infusions of 6-OHDA, 5,6-DHT, and 5,7-DHT were compared to those of nonspecific electrolytic lesions and copper sulfate infusions. Results indicate that the neurotoxins do cause nonspecific damage, but that 6-OHDA and 5,7-DHT are specific enough to provide an advantage over other methods in obtaining information on the function of catecholamine and indoleamine systems. 32 references. (Author abstract modified)

002561 Maruyama, Yuji; Kusaka, Masaru. Section of Biochemical Pharmacology, Japan Upjohn Research Laboratories, Takasaki, Gunma 370, Japan **Assay of norepinephrine and dopamine in the rat brain after microwave irradiation.** Life Sciences (Oxford). 23(15):1603-1608, 1978.

Rapid inactivation of enzymes prior to the assay of Sprague-Dawley rat brain catecholamines was evaluated. Regional levels of norepinephrine and dopamine were measured by high performance liquid chromatography with electrochemical detection after enzyme inactivation by microwave irradiation at 1.3or 5kw. Regional levels of catecholamines found after microwave irradiation differed significantly from those obtained after decapitation, indicating that rapid inactivation of brain enzymes is necessary for accurate analysis of catecholamines in rat brain. 26 references. (Author abstract modified)

002562 Newton, David W. Department of Pharmaceutics, Massachusetts College of Pharmacy, Boston, MA 02115 **Potential source of error in official diazepam assays.** Journal of Pharmaceutical Sciences. 67(4):550-551, 1978.

A possible source of interference by a benzophenone hydrolysis product with the United States Pharmacopeia (USP) spectrophotometric determination of diazepam in dosage forms is reported. The official USP assay procedure for diazepam dosage forms are not able to adequately differentiate intact diazepam from its final aromatic hydrolysis product. A minor modification of the offical assay procedure is proposed to correct this error. 10 references. (Author abstract modified)

002563 Raichle, M. E.; Grubb, R. L., Jr.; Higgins, C. S. Division of Radiation Sciences, Mallinckrodt Institute of Radiology, St. Louis, MO 63110 **Measurement of brain tissue carbon dioxide content in vivo by emission tomography.** Brain Research (Amsterdam). 166(2):413-417, 1979.

A low risk, quantitative method of measuring regional brain tissue carbon dioxide content in vivo is described. The method employs positron emission tomography to externally measure the regional concentration of (11C)labeled carbon dioxide in brain, where it exists mainly in the form of dissovled carbon dioxide and bicarbonate. Studies in rhesus monkeys confirmed the applicability of this method to the quantitivative, in vivo exploration of brain tissue acid/base chemistry. This method can be used with a variety of radiochemicals to explore the chemical properties or any organ of the body. The study of tissue drug levels with positron emission tomography could refine appraisals of the therapeutic efficacy of specific drugs and permit in vivo, regional study of specific brain receptors i humans. 15 references.

002564 Sakai, M.; Swartz, Barbara E.; Woody, C. D. Primate Research Institute, Kyoto University, Kyoto, Japan **Controlled micro release of pharmacological agents: measurements of volume ejected in vitro through fine tipped glass microelectrodes by pressure.** Neuropharmacology (Oxford). 18(2):209-213, 1979.

The amounts of substances delivered by applying pressure to fine, theta type, fluid filled glass microelectrodes were quantitated in vitro measurements. Relationships between the volumes ejected, the duration of pressure application, and tip size were investigated. Relatively consistent, reproducible delivery was found for electrodes with tips between 0.6and 1.2mcm, and the volumes of fluid ejected increased linearly with time. Results indicate that the pressure microinjection method affords more predictable quantitative delivery than the iontophoretic method. Femtomolar amounts of pharmacologically active substances could be administered by the pressure microinjection method. 16 references. (Author abstract modified)

002565 Sanberg, Paul R.; Pisa, Michele; McGeer, Edith G. Kinsmen Laboratory of Neurological Research, Department of Psychiatry, University of British Columbia, Vancouver, B. C. V6T 1W5, Canada **Strain differences and kainic acid neurotoxicity.** Brain Research (Amsterdam). 166(2):431-435, 1979.

The neurotoxicity of unilateral intrastriatal injections of 2.5or 5.0nmol kainic acid (KA) was examined in male Wistar albino, Sprague-Dawley albino, and Chester-Beatty hooded rats. A significantly greater decrease in protein content of the injected neostriatum was found in Wistar rats than in Chester-Beatty rats. A significant effect of strain on decreases in choline acetyltransferase (CAT) and glutamic acid decarboxylase (GAD) activities in the injected neostriata was also observed; this effect resulted primarily from a significantly smaller decrease of both enzymes in Sprague-Dawley rats than in the other two strains. Both enzymes decreased significantly more in rats treated with the higher dose of KA, with no significant interaction of strain with either measure. Strain effects were also found in the enzymatic activities of the noninjected neostriata; Sprague-Dawley rats had significantly less CAT activity than Wistar or Chester-

Beatty rats, and Sprague-Dawley and Chester-Beatty rats had less GAD activity than Wistar rats. These findings emphasize the importance of genetic differences in biochemical response to KA lesions. 16 references.

002566 Schaefer, Gerald J.; Holtzman, Stephen G. Biological Psychiatry Research Unit, Room 504N, Georgia Mental Health Institute, Atlanta, GA **Free-operant and auto-titration brain self-stimulation procedures in the rat: a comparison of drug effects.** Pharmacology Biochemistry and Behavior. 10(1):127-135, 1979.

The reinforcement efficacy of catecholaminergic drugs was examined in auto-titration and free-opearnt self-stimulation paradigms. Male CFE rats were implanted with bipolar stimulating electrodes aimed at the medial forebrain bundle of the lateral hypothalamus. In the free operant procedure, each lever-press produced a 200msec train of electric pulses at a suprathreshold current of constant intensity. In the auto-titration procedure, each response produced an electrical stimulus initially set at suprathreshold intensity; every 15th response reduced the stimulation current by 3mcA. The animal could reset the current to its initial intensity by pressing a second lever in the test chamber. The average current at which the rat pressed the reset lever was defined as the reinforcement threshold. This threshold was decreased by d-amphetamine and l-amphetamine, increased by haloperidol, and not changed by alpha-methyltyrosine. These effects on reinforcement threshold were not consistently related to the drug-induced changes in response rate in either procedure. Results indicate that the auto-titration procedure may be useful for distinguishing between drugs that cause nonspecific changes in the rate of ongoing behavior and those that specifically modify the reinforcement efficacy of brain stimulation. 27 references. (Author abstract modified)

002567 Schorderet, Michel; McDermed, John. McDermed: Dept. of Chemistry, Wellcome Research Laboratories, Research Triangle Park, NC 27709 **Dopamine-mimetic activity of some aminotetralins, as revealed by the production of cyclic AMP in rabbit retina in vitro.** Advances in Biochemical Psychopharmacology. 19:351-355, 1978.

The dopamine mimetic activity of several aminotetralins was studied by measuring the production of cyclic adenosine monophosphate in rabbit retina in vitro. Three of the aminotetralins were potent dopamine agonists in this model. This may prove satisfactory for rapid screening of agents interacting with presynaptic or postsynaptic dopamine receptors. 11 references.

002568 Skolnick, Phil; Goodwin, Frederick K.; **Paul, Steven M.** Laboratory of Preclinical Studies, National Institute of Alcohol Abuse and Alcoholism, Rockville, MD 20857 **A rapid and sensitive radioreceptor assay for benzodiazepine in plasma.** Archives of General Psychiatry. 36(1):78-80, 1979.

A rapid and sensitive radioreceptor assay for measuring benzodiazepines in plasma is described. This method is based on the competition between tritiated diazepam and pharmacologically active benzodiazepines present in plasma, for binding sites on rat brain synaptosomal membranes. No interference was obtained with drug free plasma of plasma samples containing high concentrations of other commonly used drugs. High correlations were obtained between the diazepam equivalents measured in plasma with the radioreceptor assay and the levels of diazepam and nordiazepam obtained by gas liquid chromatography. It is concluded that the radioreceptor assay is rapid, sensitive, specific, and requires no sophisticated equipment or methods. It should therefore prove useful in monitoring blood benzodiazepine levels for both therapeutic and toxicologic purposes. 9 references. (Author abstract)

002569 Wilcox, Richard E.; Riffee, William H.; Smith, Robert V. Dept. of Pharmacology, College of Pharmacy, University of Texas, Austin, TX 78712 **Videotaping: the evaluation of stereotypic effects of antiparkinsonian agents.** Pharmacology Biochemistry and Behavior. 10(1):161-164, 1979.

The relative accuracy of classical and videotape methods of rating the stereotypic effects of putative antiparkinsonian agents in rats was evaluated. Results indicate that the videotape technique minimized experimental bias through the use of blind ratings and increased rating accuracy through use of within/animal and between/animal controls. Permanent videotape records permitted training of raters to high efficiency, as well as direct comparisons of different rating scales under identical experimental conditions. 17 references. (Author abstract modified)

CLINICAL PSYCOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

002570 Claghorn, James L.; Mathew, Roy J.; Mirabi, Mohsen. 1300 Moursund Avenue, Houston, TX 77030 **Penfluridol: a long acting oral antipsychotic drug.** Journal of Clinical Psychiatry. 40(2):107-109, 1979.

In a 52 week double-blind study, once weekly doses of penfluridol, a diphenylbutylpiperdine derivative with a half life of 66 hours, were compared with once daily doses of chlorpromazine in 56 schizophrenic outpatients receiving maintenance treatment. Both drugs were similarly effective in the control of psychotic symptoms over an extended period of time. While no major side effects occurred with either drug, central nervous system effects were reported by 21 penfluridol and 9 chlorpromazine subjects. Advantages of once weekly dosing are noted. 3 references. (Author abstract modified)

002571 Cole, Jonathan O.; Pope, Harrison G., Jr.; LaBrie, Richard; Ionescu-Pioggia, Martin. Psychopharmacology Section, Alcohol and Drug Abuse Research Center, McLean Hospital, Belmont, MA 02178 **Assessing the subjective effects of stimulants in casual users: a methodology and preliminary results.** Clinical Pharmacology and Therapeutics. 24(2):243-252, 1978.

To assess the subjective effects of nefopam, a new nonopiate analgesic, a study was designed using 22 highly educated, young, middle to upper class subjects in a naturalistic setting. Results suggest that the design is capable of differentiating variations in subjective drug effects. On a number of measures, 10mg of d-amphetamine, a modest dosage, could be distinguished from placebo, showing changes in the direction expected for stimulant drugs. Nefopam (90mg), on the other hand, showed few differences from placebo or caffeine (300mg). Nefopam appeared mildly dysphoric, rather than stimulant, in subjective effects. 19 references. (Author abstract)

002572 Dubnitskaya, E. B.; Basov, A. M. 3-e Klinicheskoye otdeleniye, Institut psikhiatrii AMN SSSR, Moscow, USSR /**The use of phenazepam in the treatment of neurotic conditions.**/ Primeneniye fenazepama pri terapii nevroticheskikh sostoyaniy. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 78(9):1382-1387, 1978.

One hundred patients suffering from neurotic conditions were treated with the new Soviet developed tranquillizer phenazepam, a derivative of benzodiazeprine. All had been treated previously with either activan (lorazepam) or diazepam (seduxen). Daily internal doses varied from 0.5mg to 10.0mg and the duration of treatment was from 2 wk to 3 mo. The treatment proved beneficial in 82% of the cases, and in 53% it was judged to have a significant positive affect on the treatment. The best results were obtained in the treamtent of generalized hystero-neurotical states. Treatment of neurotic conditions with affective disorders was less effective. Obsessive-phobic syndromes were treated least successfully with phenazepam. A hypnotic effect similar to that of eunetics was observed. It is concluded that phenazepam is effective in the treatment of neurotic conditions. 18 references. (Journal abstract modified)

002573 Goldberg, Harold L.; Finnerty, Richard J. 26 Central Avenue, Hyde Park, MA 02136 **Comparative efficacy of tofisopam and placebo.** American Journal of Psychiatry. 136(2):196-199, 1979.

The comparative efficacy of tofisopam, a new psychopharmacological agent marketed in Europe, and placebo was evaluated in a 4 week double-blind trial in 57 anxious and/or depressed outpatients. On the basis of physician ratings and patient self-ratings, tofisopam was found to be an effective anxiolytic agent for these patients. Side-effects were reported by 21% of subjects receiving tofisopam and 10% of those receiving placebo. The drug was found to be especially effective in the treatment of somatic symptoms such as insomnia, and respiratory, gastrointestinal, automonic, and genitourinary symptoms. 9 references. (Author abstract modified)

002574 Grunberger, J.; Saletu, B.; Linzmayer, L.; Kalk, A.; Berner, P. Section of Pharmacopsychiatry, Psychiatric University Clinic, Vienna, Austria **Pharmacodynamic investigations with WE 941, a new triazolodiazepine, by means of psychometric analyses.** Current Therapeutic Research. 24(4):427-440, 1978.

The psychoactivity and pharacodynamic properties of WE 941, a new triazolothienodiazepine, were investigated in 10 normal volunteers by means of psychometric methods. In a double-blind, placebo controlled study the subjects received in randomized order, at weekly intervals, single oral doses of 0.1, 0.3and 0.5mg WE 941, placebo, and 30mg fluazepam as a reference drug. Evaluations were made before as well as 2, 4, 6, and 8 hours after administration and included measurements of attention, concentration, attention variability, motor performance, reaction time, flicker fusion threshold, after effect, mood, and affectivity. Placebo produced only one statistically significant change: a deterioration in attention variability in the 6th hour after administration. By contrast, WE 941 and flurazepam showed significant psychoactivity starting in the 2nd hour, which peaked in the 4th hour after administration and slowly decreased thereafter. Significant changes were still seen 8 hours after WE 941. A WE 941 dose of 0.3mg seems to equal in potency 30mg flurazepam. The findings suggest that 0.1mg is the minimal psychoactive dose, which has a tranquilizing effect, while 0.5mg WE 941 exerts a strong sedative effect and may be regarded as a hypnotic dose. 17 references. (Author abstract)

002575 Jorgensen, Aksel. Biochemical Department, H. Lundbeck & Co., A/S DK-2500 Valby-Copenhagen, Denmark **A sensitive and specific radioimmunoassay for cis(Z)-flupenthixol in human serum.** Life Sciences (Oxford). 23(15):1533-1542, 1978.

The injection of cis(Z)-7-carboxy-flupenthixol covalently bound to bovine serum albumin into a sheep produced an antibody serum which was combined with tritium labeled cis(Z)-flupenthixol in a radioimmunoassay for cis (Z)-flupenthixol. The assay had a limit of sensitivity of about 0.3ng/ml serum or plasma. Some cross-reactivity was seen with trans(E)-flupenthixol, flupenthixol metabolites, and cis(Z)-flupenthixol esters, but this did not influence the estimation of cis(Z)-flupenthixol to a significant degree. A series of drugs structurally related to flupenthixol showed varying degrees of cross-reactivity, whereas compounds of other therapeutic groups showed very little. The standard deviation was 6-7% when a series of identical samples of pooled patient sera was estimated. Following oral administration to human volunteers, cis(Z)-flupenthixol was absorbed slowly, with maximum serum level 6 hours after administration. Intramuscular injection of flupenthixol decanoate in Viscoleo yielded serum concentration curves with maxima 7 days after injections and a twofold fluctuation in serum level in a 2 week dosage interval. 4 references. (Author abstract modified)

002576 Lemberger, Louis; Rowe, Howard; Carmichael, Ralph; Oldham, Samuel; Horng, Jong S.; Bymaster, Frank P.; Wong, David T. Lilly Lab. for Clinical Research, Indianpolis, IN

46202 **Pharmacologic effects in man of a specific serotonin-reuptake inhibitor.** Science. 199(4327):436-437, 1978.

The pharmacologic effects of a specific serotonin reuptake inhibitor, fluoxetin, was investigated. Fluoxetine caused a 63% inhibition of (3H) serotinin uptake into platelets obtained from normal volunteers to whom the drug was administered (30mg daily) for 7 days. This dose had no effect on the usual pressor response produced by injections of norepinephrine or tyramine. Results indicate that fluoxetine is a specific inhibitor of serotonin reuptake and suggest that it may be useful in evaluating the role of serotonin in the pathophysiology of mental diseases. Furthermore, the drug may be a potential therapeutic agent in treating these disorders. 6 references. (Author abstract modified)

002577 Lerner, Y.; Lwow, E.; Levitin, A.; Belmaker, R. H. Eitanim Government Hospital, Jerusalem, Israel **Haloperidol vs. diazepam in the first 24 h of treatment of psychosis: a controlled study.** Israel Journal of Medical Sciences (Jerusalem). 14(9):1003, 1978.

A summary of a paper read at the 41st Meeting of the Israel Physiological and Pharmacological Society held March 1978, in Jerusalem is presented. A controlled double-blind randomized trial of high doses parenteral haloperidol vs. high dose parenteral diazepam, a benzodiazepine minor tranquilizer thought to be devoid of antipsychotic effects, is presented. After 2 days observation of drug free patients, 20 newly admitted psychotic patients received a total of 20 to 35mg of haloperidol i.v. and 20 patients received a total of 30 to 40mg of diazepam i.v. Ratings at 4 and 24 hours with the Brief Psychiatric Rating Scale revealed significant improvement in both groups but no significant differences between the two treatments. It is concluded that the specific antipsychotic effect of haloperidol does not occur within the first 24 hours of treatment. A therapeutic effect common to diazepam and to haloperidol does appear within the first 24 hours of treatment. (Author abstract modified)

002578 Lieberman, Abraham N.; Kupersmith, Mark; Gopinathan, Govindan; Estey, Eli; Goodgold, Albert; Goldstein, Menek. Neurology, New York University Medical Center, 566 First Avenue, New York, NY 10016 **Bromocriptine in Parkinson disease: further studies.** Neurology. 20(3):363-369, 1979.

In a clinical trial, bromocriptine was administered to 66 patients with advanced Parkinson disease (PD) and increasing disability despite optimal treatment with levodopa/carbidopa (Sinemet). Forty-five patients tolerated at least 25mg per day of bromocriptine (the adequately treated group) in addition to Sinemet and had significantly decreased rigidity, tremor, bradykinesia, gait disturbance, and total score, but increased involuntary movements. Bromocriptine was discontinued in 29 of 66 patients because of adverse effects, including mental changes (14 patients) and involuntary movements (9 patients). Despite adverse effects, expense, and scarcity, bromocriptine, when added to levodopa, is useful in patients with advanced disease who no longer respond satisfactorily to levodopa, and for whom no other treatment is available. 72 references. (Author abstract modified)

002579 Maryanoff, Bruce E.; Zelesko, Michael J. Chemical Research Department, McNeil Laboratories, Inc., Fort Washington, PA 19034 **Stereochemical considerations in structural comparison of enkephalins and endorphins with exogenous opiate agents.** Journal of Pharmaceutical Sciences. 67(4):590-591, 1978.

Stereochemical considerations in the structural comparison of enkephalins and endorphins with exogenous opiate agents are discussed in relation to the tyramine hypothesis. The structure/activity relationship between morphine and methionine-enkephalin is marked by a reversal in stereospecificity. Analogous stereochemical inversion in structure/activity relationships are found in diphenylpropylamine and certain anilide analgesics and may generally be interpreted in terms of differing substrate/receptor interactions or induced fit theories. It is concluded that any model proposing to rationalize the structure/activity relationships of opiates must consider stereochemical inversion phenomena. 36 references.

002580 McCurdy, Layton. Dept. of Psychiatry and Behavioral Sciences, Medical University of South Carolina, 171 Ashley Ave., Charleston, SC 29403 **Lorazepam, a new benzodiazepine derivative, in the treatment of anxiety: a double-blind clinical evaluation.** American Journal of Psychiatry. 136(2):187-190, 1979.

The efficacy of the new benzodiazepine derivative, lorazepam, in the treatment of anxiety was examined in a double-blind clinical evaluation of 95 adult outpatients suffering from moderate to severe anxiety. Patients were evaluated at pretreatment and after 2 and 4 weeks of treatment, using three rating scales. Lorazepam, at an average daily dose of 3.2mg twice daily, was found to be highly effective in relieving anxiety as documented by clinically and statistically significant differences over placebo in most of the items on all rating scales at all rating periods. No serious adverse effects were reported, and there were no adverse interactions with other medications, including digitalis and aspirin. 9 references. (Author abstract modified)

002581 Pena-Ramos, Abelardo; Muniz, Carlos; Goodman, Lowell I.; Borgen, Lowell A. Department of Psychiatry, University of South Florida, Tampa, FL 33620 **Controlled comparison of trebenzomine with doxepin as an antidepressant-anxyiolytic.** Journal of Clinical Psychiatry. 40(2):104-106, 1979.

Trebenzomine, a new psychotropic drug, was compared with doxepin in a double-blind controlled study of 26 neurotic inpatients with depression and/or anxiety. Multiple ratings by physician, nurse, and patients all concurred that both drugs produced significant improvement in anxious and depressive symptomatology over the 3 week trial period. No significant differences were found between the two drugs either in terms of rate or degree of improvement of incidence of side effects. Further investigation of trebenzomine in the treatment of anxious depression is warranted. 13 references. (Author abstract)

002582 Varner, R. V.; Hu, J. T.; Beller, S. A. Texas Research Institute on Mental Sciences, Houston, TX 77030 **Use of new non-tricyclic antidepressant drug in elderly depressed psychiatric patients.** Gerontological Society: 31st Annual Scientific Meeting. 18(5, Part 2):135, 1978.

A summary of a paper read at the 31st Annual Meeting of the Gerontological Society, held in Dallas , November 1978, is presented. To evaluate the effectiveness of Nisoxetine ((3-(0-methoxyphenoxyl)-N-methyl-3-phenylpropylamine HCL) a new nontricyclic antidepressant preparation, a group of elderly depressed women were treated with the drug over a 4 week period within the setting of a geropsychiatric inpatient service. Preliminary test data revealed that Nisoxetine was effective as an antidepressant compound, though almost totally devoid of anticholinergic side-effects. No confusion, notable EKG changes, complaints of constipation, or other notable anticholinergic side-effects were observed during the clinical trial. (Author abstract modified)

08 DRUG TRIALS IN SCHIZOPHRENIA

002583 Arrojo-Lois, M. Clinica de Enfermedades Nerviosas y Mentales, Santiago de Compostela, Spain /**Clinical experiences accomplished with the neuroleptic 19.366 R.P. (pipotiazine)./** Experiencias clinicas efectuadas con el neuroleptico 19.366 R.P.

(pipotiazina). Acta Luso-Espanolas de Neurologia, Psiquiatria y Ciencias Afines (Madrid). 6(3):309-312, 1978.

The effects of pipotiazine, a neuroleptic with prolonged action, used to improve psychotic symptomatology, were studied. The drug was evaluated independent of the initial trial phase, to discover the benefits of prolonged treatment. Twenty-seven patients, 15 men and 12 women, were selected. Their ages were between 19 and 58 years. There were seven cases of simple schizophrenia, nine of paranoid schizophrenia, six of catatonic schizophrenia, one of psychoneurosis, three of hypertimica, and one of depression. The doses administered varied, depending on the individual. The administrations lasted for a year and a half. The action of the drug was studied and it was found that a small dose acted as an uninhibitor and a higher dose showed the effects of an antipsychotic. In only one case was suspension of treatment necessary. Results show that the highest doses brought about a higher percentage of favorable remissions. It is concluded that with weak doses, pipotiazine has the effect of an uninhibitor, but with an increase in the dose an antipsychotic effect is achieved. Pipotiazine also shows good tolerance, with the exception of one suspension of treatment in the evaluation. 8 references.

002584 Crow, T. J. Division of Psychiatry, Clinical Research Centre, Watford Rd., Harrow, Middlesex HA1 3UJ, England **Clinical Research Centre Division of Psychiatry 1974-1977.** Psychological Medicine (London). 8(3):515-523, 1978.

The main areas of research undertaken by the Clinical Research Centre Division of Psychiatry in England since its establishment in 1974 are reviewed. Research studies have been conducted on: 1) elucidating the mechanism of action of neuroleptic drugs in acute schizophrenia; 2) investigating the nature of the psychological deficit in chronic schizophrenia and its correlates; 3) postmortem studies of monoamine and other neurohumoral mechanisms in schizophrenia; and 4) animal studies of the functions of specific neurohumoral systems, and in developing animal models of functional psychoses. 72 references. (Author abstract modified)

002585 Crow, T. J.; Johnstone, E. C.; Longden, A.; Owen, F. Division of Psychiatry, Clinical Research Center, Northwick Park Hospital, Harrow Middlesex HA1 3UJ, England **Dopamine and Schizophrenia.** Advances in Biochemical Psychopharmacology. 19:301-309, 1978.

The hypotheses that some of the symptoms of schizophrenia arise from excessive dopaminergic activity and that the effects of this excess can be reduced by the dopamine receptor blockade induced by neuroleptics are discussed. Studies of the effects of the isomers of flupenthixol in schizophrenic patients indicate that the antipsychotic action of the neuroleptics is due to dopamine receptor blockade. However, the time course of the therapeutic effect suggests that the dopamine receptor blockade is not directly related to clinical improvement, but may be a necessary condition for other slower changes to take place. Moreover, neuroleptics therapy reduced delusions, hallucinations, and thought disorders, but had no apparent affect on affective symptoms. Biochemical studies have cast doubt on the dopamine overactivity hypothesis of schizophrenia, and the observation that schizophrenic and parkinsonian symptoms can coexist suggests that increased dopamine release is not necessary for the expression of schizophrenic illness. Preliminary studies of postmortem brains from schizophrenic patients and controls provide no evidence for increased dopaminergic activity in the schizophrenics, but suggest the possibility of a disturbance in the relationship between gamma-aminobutyric acid and dopamine neurons in the nucleus accumbens. 26 references. (Author abstract modified)

002586 Donlon, Patrick T.; Meadow, Arnold; Tupin, Joe P.; Wahba, Michael. 2252 45th Street, Sacramento, CA 95817 **High vs standard dosage fluphenazine HCL in acute schizophrenia.** Journal of Clinical Psychiatry. 39(11):800-804, 1978.

The efficacy and safety of using an oral rapid or neuroleptization method (maximum 80mg/day) verses fixed standard dosage (20 mg/day) fluphenazine were compared. Thirty-two hospitalized, acutely decompensated schizophrenic patients, each over a maximum period of seven days, were studied. The data were collected using the Benjamin Proverb Test and rating scales for psychopathology and adverse effects. Since few significant differences were found, it is concluded that the rapid neuroleptization method is not superior to the fixed standard dosage method in treating acute schizophrenia. 9 references. (Author abstract modified)

002587 Engelhardt, David M.; Rudorfer, Leon; Rosen, Bernard. 450 Clarkson Avenue, Brooklyn, NY 11203 **Haloperidol and thiothixene in the long-term treatment of chronic schizophrenic outpatients in an urban community: social and vocational adjustment.** Journal of Clinical Psychiatry. 39(12):834-840, 1978.

The comparative effectiveness of haloperidol and thiothixene in facilitating vocational and social adjustment, as well as controlling more traditionally studied psychopathological variables, was examined in a 24 week double-blind study of 36 urban chronic schizophrenic outpatients. Significant improvement favoring thiothixene was shown physicians' ratings, ratings by relatives living in the same household as the patient, and patients' self-ratings. Side-effects occurred with similar frequency in both drug groups; no patients were required to discontinue therapy because of side-effects. There were no significant clinical abnormalities in laboratory values of either group. 24 references. (Author abstract modfied)

002588 Fierri, Alberto Manuel; Galvan, O.; Scovenna, R.; Loaiza, S.; Blumeswild, A. Clinica Psiquiatrica, Hosp. Nac. ""Jose T. Borda," Buenos Aires, Argentina /**Evaluation of the clinical effect of penfluridol on schizophrenics.**/ Evaluacion del efecto clinico del penfluridol en esquizofrenicos. Neuropsiquiatria (Buenos Aires). 9(1):37-39, 1978.

The clinical effects of penfluridol were investigated in 24 male chronic hospitalized schizophrenics, with an average age of 37.4years. Only patients with a possibility of stabilization and control of the illness were chosen. Previous medications consisted of various drugs and electric shock; these were discontinued at the outset of the experiment. Each patient was given an oral dose of 20 to 40mg of penfluridol, depending on previous doses of neuroleptic medication. The doses were adapted weekly to provide the optimum individual level, and treatment lasted between 3 and 7 months. Results show that a marked improvement was achieved in 76% of the patients, and that tolerance of the drug was acceptable. It is recommended that penfluridol be used for maintenance therapy for these types of patients. 8 references. (Journal abstract modified)

002589 Gardos, George; Tecce, Joseph J.; Hartmann, Ernest; Bowers, Penelope; Cole, Jonathan O. IRR-233 Boston State Hospital, 591 Morton Street, Boston, MA 02124 **Treatment with mesoridazine and thioridazine in chronic schizophrenia: II. potential predictors of drug response.** Comprehensive Psychiatry. 19(6):527-532, 1978.

A single-blind study of the treatment of refractory hospitalized schizophrenics with auditory hallucinations with mesoridazine and/or thioridazine is evaluated in terms of prediction of selective drug responders. Results indicate that the typical mesoridazine responder is a female, with a diagnosis of paranoid schizophrenia and who, despite high dosages of neuroleptics,

shows auditory hallucinations and an abundance of thought disorders, rather than anergia, and poor social functioning. Prior to mesoridazine treatment, mesoridazine responders tend to awaken often during the night. Explanations of selective drug responsivity are discussed. 16 references.

002590 Gardos, George; Tecce, Joseph J.; Hartmann, Ernest; Bowers, Penelope; Cole, Jonathan O. IRR-323, Boston State Hospital, 591 Morton Street, Boston, MA 02124 **Treatment with mesoridazine and thioridazine in chronic schizophrenia: I. Assessment of clinical and electrophysiologic responses in refractory hallucinating schizophrenics.** Comprehensive Psychiatry. 19(6):517-525, 1978.

A double-blind, crossover study of the therapeutic efficacy and clinical and electrophysiologic responses in refractory hallucinating schizophrenics of mesoridazine and thioridazine, is described. Mesoridazine showed a modest superiority over thioridazine after 12 weeks of drug treatment, with a significant difference in composite clinical score between the two drugs. The pattern of changes on mesoridazine was mostly the same as on thioridazine, except on neuropsychologic tests, where a differential drug response was observed. 20 references.

002591 Gillis, John S. Oregon State University, Corvallis, OR 97331 **Antipsychotic drugs and conflict resolution: a study of the comparative effects of trifluoperazine, haloperidol, and thioridazine.** Research Communications in Psychology, Psychiatry and Behavior. 4(1):3-20, 1979.

The effects of three autopsychotic agents (trifluoperazine, haloperidol, thioridazine) on the abilities of schizophrenic patients to resolve cognitive differences in a joint problem-solving situation were examined. Thirty-four hospitalized schizophrenics were selected for inclusion in the study on the basis of their ongoing chemotherapy regimens. These subjects were divided into four treatment groups based on their major therapeutic drugs and supplementary medications. Conflict resolution was evaluated by means of a series of interactive judgment tasks. The several performance indices derived from these tasks indicated no differences between treatments. There was, however, a consistent although nonsignificant tendency for haloperidol patients to perform better than thioridazine subjects on most performance indices. 12 references. (Author abstract)

002592 Gottschalk, Louis A.; Dinovo, Eugene C.; Nandi, Bina R. Dept. of Psychiatry and Human Behavior, College of Medicine, University of California at Irvine, Irvine, CA 92664 **Cerebrospinal fluid concentration of thioridazine and its metabolites in schizophrenic patients.** Research Communications in Psychology, Psychiatry and Behavior. 3(2):83-87, 1978.

An experiment was conducted to measure the relationship of plasma concentrations of thioridazine and its metabolites to cerebrospinal fluid (CSF) concentrations of acute schizophrenic patients while these patients were on a continous daily antipsychotic medication of oral doses (4mg/kg) of thioridazine. The levels of thioridazine and its metabolites in both plasma and CSF were measured by the spectrofluormetric method of Pacha (1969) and the gas chromatographic (GLC) method of Dinovo et al (1976) in three patients. Results indicate that the CSF samples of the patients barely showed presence of the drug or its metabolites, using both the spectrofluormetric and CLC methods of assay, though plasma levels of the drug and its metabolites were measurable. It is likely, however, that the drug and its metabolites were present in the CSF at levels below the sensitivity of the assay methods used. Possible reasons for the low levels of thioridazine and its metabolites in the CSF of the schizophrenic patients are discussed. 5 references.

002593 Hurt, Stephen Wayne. University of Chicago **Longitudinal assessment of schizophrenic thought disorder. (Ph.D. dissertation).** Dissertation Abstracts International. 39(6):2988-B, 1978. (Not available from Univ. Microfilms), 1978.

The utility of two pharmacological strategies in producing remission of thought disorders in a group of schizophrenic patients was assessed in a double-blind, longitudinal study. Patients in the treatment groups (various regimins of haloperidol) were rated by two psychiatrists and a psychiatric social worker on the Brief Psychiatric Rating Scale, and the Clinical Global Index at baseline, days one, three and five of treatment and from one to three times weekly for the remaining two weeks of the study. Significant change was found in the average Thought Disorder Index scores of the treatment groups but not the placebo control group. Prior to treatment, the mean level of thought disorder in the patient groups was significantly elevated over that found in the normal control. After three weeks of haloperidol intervention, the treatment group patients showed residual levels of thought disorder significantly higher than those found on second testing in the normal control group. The change seen in the treatment groups was proportional to that seen in the normal controls, the latter change being attributable to anxiety reduction and, perhaps, practice effects. (Journal abstract modified)

002594 Kurilova, I. I.; Lideman, R. R. Laboratoriya obshchey patofiziologii, Institut psikhiatrii AMN SSSR, Moscow, USSR / **Decrease in monoamine oxidase activity of thrombocytes of schizophrenic patients./** Snizheniye aktivnosti monoaminoksidazy trombotsitov bol'nykh shizofreniyey. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 78(9):1351-1354, 1978.

The activity of monoamine oxide on the thrombocytes of schizophrenic patients was studied in 28 schizophrenic Ss and 36 healthy Ss. The activity decreased by 14% in the schizophrenic Ss. In female schizophrenic Ss, the activity was not significantly different from normal, however in male schizophrenic Ss it differed considerably. A correlation with positive disorders was not noted. These findings contradict the results of several other researchers. 18 references. (Journal abstract modified)

002595 Luchins, D.; Ban, T.A.; Lehmann, H.E. Baallan Memorial Institute, McGill University, Montreal, Quebec, Canada **A review of nicotinic acid, N-methylated indoleamines and schizophrenia.** International Pharmacopsychiatry (Basel). 13(1):16-33, 1978.

The hypothesis that endogenously formed N-methylated metabolites of indoleamines may play a role in the pathogenesis of schizophrenia is reviewed. Although N-methylated indoleamines can be produced in vivo and have significant psychotomimetic effects, there is little evidence for a specific increase in the methylation of indoleamines in schizophrenic patients. It is noted that even if the relationship between schizophrenia and N-methylated indoleamines exists, nicotinic acid is not an appropriate therapeutic agent. 102 references. (Author abstract)

002596 Noguera Hosta, Ramon; Rendueles de Olmedo, Guillermo. Hospital Psiquiatrico de Girona, Girona, Spain **/Seven years of experience with ""long-lasting" neuroleptics./** Siete anos de experiencia con neurolepticos ""retard." Acta Luso-Espanolas de Neurologia, Psiquiatria y Ciencias Afines (Madrid). 6(3):293-298, 1978.

The clinical results obtained in using ""depot" phenothiazines in treating outpatients are discussed. A scale was established before the experiment: very good, good, regular, and negative. A total of 53 outpatients, 27 men and 26 women, were chosen. Their ages were between 7 and 71. The distribution of their

mental illnesses are as follows: 45 cases of schizophrenic psychosis, 7 cases of mixed psychosis, and 4 of oligophrenic conduct disturbances. Four long-lasting neuroleptics, eutimox, modicate, Mi-Lonseren, and Lonseren, were administered, the doses varying with each individual. Results show that of 53 cases, 32 fell between good and very good on the scale, and the other 21 cases between regular and negative, from which it is concluded that the use of long-lasting neuroleptics is acceptable. The use of these neuroleptics is not the solution to the problem of psychotic illnesses. Secondary effects of the long-lasting neuroleptics and the new relational field of the doctor-patient-family triad the drugs have brought about are discussed. 16 references.

002597 Panteleyeva, G. P.; Tsutsul'kovskaya, M. Ya.; Mazurskiy, M. B.; Danilenko, Yu. M. Institut psikhiatrii AMN USSR, Moscow, USSR **/Long-term treatment of schizophrenia patients with leponex (chlozapine)./** Dlitel'noye lecheniye leponeksom (klozapinom) bolinykh shizofreniyey. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 78(8):1247-1256, 1978.

The long-term effects of leponex were studied in 23 schizophrenic Ss who had been treated over a 4 year period. The influence of leponex on the frequency and duration of relapses, the dynamics of disorders and social adaptation were studied. Ss were chosen who had been treated unsuccessfully with other methods prior to treatment with leponex. At the beginning of treatment all Ss suffered acutely, and personality changes were severe enough to affect work productivity. Ss were physically healthy and the average length of their disease was 13.5years. Data indicate that leponex arrests acute psychoses and alleviates the clinical signs and frequency of relapses. Its suitability for prolonged use is due to the minor side-effects it produces. 15 references. (Journal abstract modified)

002598 Rickels, Karl; Byrdy, Harold; Valentine, John; Postel, William; Norstad, Norman; Downing, Robert. 203 Piersol Building, University Hospital, 3400 Spruce Street G1, Philadelphia, PA 19104 **Double-blind trial of thiothixene and chlorpromazine in acute schizophrenia.** International Pharmacopsychiatry (Basel). 13(1):50-57, 1978.

To compare the efficacy and safety of the two drugs in treating schizophrenia, a double-blind trial of chlorpromazine and thiothixene was conducted with 79 acutely ill, newly hospitalized schizophrenic patients. Both drugs were equally effective at mean dosages of 44.3mg for thiothixene and 926mg/day chlorpromazine, in producing meaningful symptomatic improvement over an average period of appriximately 3 weeks, as measured by global assessment (CGI), the Brief Psychiatric Rating Scale (BPRS), and the Nurse's Observational Scale for Inpatient Evaluation (NOSIE). 9 references. (Author abstract modified)

002599 Sakurai, Y.; Nakahara, T.; Ikenaga, H.; Takahashi, R. Nagasaki University, Japan **Clinical significance of pattern of blood chlorpromazine and its metabolite levels and prediction of response to chlorpromazine treatment: studies on the rational pharmacotherapy in schizophrenics.** Psychiatria et Neurologia Japonica (Tokyo). 80(7):405-424, 1978.

The clinical significance of the pattern of blood chlorpromazine (CPZ) and its metabolite levels and prediction of response to CPZ treatment was investigated in 37 schizophrenic patients. It was found that the therapeutic response of schizophrenic patients to CPZ may be predicted from determining the blood levels of CPZ and its principal metabolites, demethylated CPZ and CPZ sulfoxide, 3 hours after administration of 50mg CPZ. 60 references.

002600 Taylor, Pamela; Gillman, P. K.; Gaind, R. Guy's Hospital, St. Thomas Street, London SE1 9RT, England **Alpha-methyldopa in schizophrenia.** Journal of Clinical Psychiatry. 39(11):815-816, 1978.

The case of a schizophrenic in whom, after an overdose of alpha-methyldopa, there was a dramatic and apparently complete resolution of psychotic symptomatology, followed after a few weeks by a sudden return of psychosis is presented. It seems possible that a dose of alpha-methyldopa one hundred times greater than usual, as in this case, prolongs the interference of dopaminergic transmission in the CNS. The value of exploring further a role for alpha-methyldopa in the treatment of some schizophrenics is suggested. 8 references. (Author abstract modified)

002601 Treffert, Darold A. Winnebago Mental Health Institute, Winnebago, WI 54985 **Marijuana use in schizophrenia: a clear hazard.** American Journal of Psychiatry. 135(10):1213-1215, 1978.

At the 130th annual meeting of the American Psychiatric Association, held in Toronto, May 1977, a paper was presented which investigates the effects of marihuana use among schizophrenic patients. The use of marihuana as the independent variable produced a serious exacerbation of a psychotic process in four schizophrenic patients whose illness was otherwise well controlled with antipsychotic medication. The sole substance abused was marihuana and antipsychotic medication intake remained constant. Each time marihuana use at moderate levels began, there was exacerbation and deterioration. It is suggested that marihuana use is a special hazard to schizophrenic patients and that physicians should alert such high risk patients to the possible untoward interaction between their illness and marihuana. 18 references. (Journal abstract modified)

002602 Tuason, V. B. University of Minnesota, Minneapolis, MN 55455 **The NIMH-PRB collaborative study of long acting fluphenazine. (Unpublished paper).** Final Report, NIMH Grant R01-MH-24969, 1978. 13 p.

The effectiveness of treatment involving use of a long acting injectable phenothiazine (fluphenazine decanoate) and treatment relying on oral medication (fluphenazine hydrochloride) for schizophrenia was determined. An attempt was also made to determine if the reemergence of symptoms is the cause of voluntary discontinuation of medication or an effect of it. Extensive data were obtained from 25 patients who completed a 1 year maintenance phase, 18 of whom entered the medication adjustment phase. Analyses of 290 patients at four collaborating hospitals indicate that patients who report high levels of neurotic symptoms are more likely to relapse if they receive depot rather than oral fluphenazine. No differences in the nature of symptoms seen at the point of relapse occur between the two treatments. The hypothesized benefits of a treatment regime involving depot administration or the expected liabilities (depression and increased side effects) were not confirmed.

002603 Wen, H. L.; Lo, C. W.; Ho, W. K. K.; Mehal, Z. D.; Ng, Y. H.; Lam, S.; Ma, L. Neurosurgical Unit, Kwong Wah Hospital, Tung Wah Group of Hospitals, Kowloon, Hong Kong **Naloxone in the treatment of schizophrenia.** Modern Medicine of Asia (Hong Kong). 14(12):51-52, 54-55, 1978.

Responses to naloxone treatment for 1 week in 10 cases of schizophrenia were examined. All but three patients showed moderate to good recovery from the classical symptoms at the end of the treatment period. CSF samples from five patients were examined for possible changes of opiate-like activity before and after naloxone treatment. A decrease of activity associated with the endorphin fraction was observed in three out of the four cases. Results support the contention that the inhibition of endorphin secretion may be the underlying mechanism of na-

loxone's action in improving symptoms associated with schizophrenia. 20 references. (Author abstract modified)

002604 Woggon, B. Forschungsdirektion, Psychiatrische Universitatsklinik, CH-8000 Zurich, Switzerland /**Penfluridol: results of a clinical trial during 1 year.**/ Penfluridol-Ergebnisse einer einjahrigen klinischen Prufung. International Pharmacopsychiatry (Basel). 13(1):1-15, 1978.

During an open clinical trial, 51 schizophrenic patients were treated with Penfluridol, 34 for 1 year and 17 for a shorter time. The mean dosage of Penfluridol was 22 to 28mg per week. Assessments were made on days 0, 14, 28, 56, 90, 180, 270, and 365 using the AMP system and the EPRS scale of Simpson and Angus. The symptomatology was reduced mainly during the first 3 months of treatment and remained relatively unchanged afterwards. Penfluridol showed a good antipsychotic effect on schizophrenic symptoms (thought disorders and paranoid symptoms, autism, and schizophrenic affective disorders). The dosage produced only a slight sedative effect and was well tolerated concerning autonomic and extrapyramidal side-effects. 19 references. (Journal abstract)

002605 Zisook, Sidney; Devaul, Richard; Jaffe, Kenneth; Click, Maurice, Jr. Post Office Box 20708, Houston, Texas 77025 **Loxapine succinate (Loxitane) in the outpatient treatment of acutely ill schizophrenic patients.** Current Therapeutic Research. 24(4):415-426, 1978.

The clinical effectiveness of loxapine succinate was evaluated during a 4 week open study with 18 otherwise healthy schizophrenic patients presenting with manifestations of an acute shhizophrenic episode or an exacerbation of chronic schizophrenia. Patients were diagnosed by research diagnostic criteria and had no better than fair prognostic ratings. Improvement was rapid, with patients showing significant changes in many items and factors of the Brief Psychiatric Rating Scale as well as Clinical Global Impression Scales as early as 48 hours after beginning treatment. All but two of the patients were maintained as outpatients throughout the study. Although mild extrapyramidal side-effects were frequently noted, the drug was well tolerated. 23 references. (Author abstract)

09 DRUG TRIALS IN AFFECTIVE DISORDERS

002606 Avery, David; Mills, Mark. Mills: Psychiatric Evaluation Unit, Veterans Administration Hospital, Palo Alto, CA 94304 **Electroconvulsive therapy and antidepressants in the treatment of depression.** In: Ayd, F., Mood disorders. Baltimore, Ayd Medical Communications, 1978. 266 p. (p. 138-153).

A paper read at the Tenth Annual Taylor Manor Hospital Scientific Symposium, held in Baltimore in April 1978, is presented. The efficacy of electroconvulsive therapy (ECT) and antidepressants in the treatment of depression are explored. Topics discussed include: random or selective sampling, the adequacy of antidepressant treatment, tricyclic antidepressant studies, monoamine oxidase inhibitor studies, and tryptophan studies. Conclusions indicate that no study shows antidepressant medication to be superior to ECT in the treatment of depression; that most studies claim the superiority of ECT to antidepressants in the treatment of endogenous depression; that there is little evidence to suggest that antidepressants in combination with ECT are better than ECT alone; and that ECT is the most effective treatment of endogenous depression, especially in those individuals with severe delusional depressions. 69 references.

002607 Ayd, Frank J., Jr.; Taylor, Irving J. Department of Professional Education and Research, Taylor Manor Hospital, Ellicott City, MD 21043 **Mood disorders: the world's major public health problem.** Baltimore, Ayd Medical Communications, 1978. 266 p.

Papers on affective disorders read at the Tenth Annual Taylor Manor Hospital Scientific Symposium, held in Baltimore, MD, in April 1978, are presented. It is argued that the prevalence of depressive disorders in a given population increases with the increase in life expectancy, the rapidly changing psychosocial environment, the increase in morbidity from chronic disease, and the increase in medicament consumption including oral contraceptives, which are potentially a significant factor contributing to depression among women. Recent advances in psychobiology, psychotherapy, drug therapy, and electroconvulsive therapy are identified and discussed. It is asserted that there is a body of knowledge which allows prevention of certain types of depression and effective treatment of most of those who have the disorder. However, only a minute proportion of those who are ill obtain adequate care, and many opportunities for prevention are not realized because of lack of resources, nonapplication of knowledge, and the absence of practical and economically feasible models of service provision suited for the different sociocultural settings and the expectations of communities. Family practice is advanced as a means for channeling gains in affective disorder therapy to patients.

002608 Bobon, D. P.; Fanielle, J.; Mormont, C.; Breulet, M.; Bobon, J. Department of Psychiatry, Rue Saint-Laurent 58, B-4000 Liege, Belgium, EEC **Time-blind videotaped evaluation of injectable diazepam, lorazepam and placebo.** Acta Psychiatrica Belgica (Bruxelles). 78(4):619-634, 1978.

Results are presented from the 5 day treatment of anxiety with 10mg diazepam, 5mg lorazepam, or saline t.i.d. Double-blind crossover conditions and iv and im injections were used with the 18 inpatients. Pretreatment/posttreatment measures in the time blind methodology included the 100 mm Visual Analogue Scale (VAS), a standard interview, and physiological measurements. The interviews were rated on three scales: the VAS, Hamilton Anxiety Scale, and an ad hoc Verbal and Non-Verbal Anxiety Scale. Results demonstrate the superiority of lorazepam over diazepam in treating psychic anxiety, somatic anxiety, sleep and blood pressure problems. The only significant side effect was drowsiness. (Journal abstract modified)

002609 Bowen, R. C. Department of Psychiatry, University Hospital, Saskatoon, Saskatchewan, Canada **The effect of diazepam on the recovery of endogenously depressed patients.** Journal of Clinical Pharmacology. 18(5-6):280-284, 1978.

Forty endogenously depressed patients given standard antidepressants and/or electroconvulsive therapy in a general hospital psychiatric ward were assessed. The short form of the Beck Depression Inventory and the Hamilton Depression Rating Scale were used. Standard therapy with tricyclic antidepressants or electric shock was determined by the patients' own psychiatrists. Results of the Beck Depression Inventory indicate that the addition of diazepam retarded the improvement of patients receiving only tricyclic antidepressants, but had no effect on the recovery of patients receiving electroconvulsive therapy. 22 references. (Author abstract modified)

002610 Brenner, Arnold; Wapnir, Raul A. 8630 Liberty Plaza Mall, Randallstown, MD 21133 **A pyridoxine-dependent behavioral disorder unmasked by isoniazid.** American Journal of Diseases of Children. 132(8):773-776, 1978.

The case study of a young child with hyperkinetic behavior that was accentuated by isoniazid therapy and controlled with massive doses of pyridoxine hydrochloride is reported. Periodic withdrawal of pyridoxine was associated with return of hyperkinesis. Metabolic studies that suggest a block in the kynurenine

pathway of tryptophan metabolism are described. The patient has been followed for 6 years and has required pharmacologic doses of pyridoxine to control her behavior. 27 references. (Author abstract modified)

002611 Brown, Walter Armin; Mueller, Barbara. Neuroendocrine Research Laboratory, Providence Veterans Administration Hospital, Davis Park, RI 02908 **Alleviation of manic symptoms with catecholamine agonists.** American Journal of Psychiatry. 136(2):230-231, 1979.

The effects of catecholamine agonists on manic symptoms were evaluated in two men with well documented histories of mania and depression. Within a week of a double-blind switch from lithium to placebo, both patients became manic. Following 10 days' treatment with placebo, the subjects received L-dopa (500mg), apomorphine (0.5mg), methylphenidate (20mg), and d-amphetamine (15mg) in a random sequence on a double-blind basis. Neither patient showed an increase in mania after administration of any of these drugs: 45 min following administration of any of these agents, speech and body movements approached normal levels. These effects lasted about 3 hrs, after which full blown manic symptoms recurred. D-amphetamine appeared most effective in alleviating symptoms. Results are discussed within the context of previous biochemical and psychopharmacological research. 7 references.

002612 Calanca, M. A. Clinique psychiatrique universitaire de Cery, CH-1008 Prilly-Lausanne, Switzerland **/Indications for mianserin in relation to its absence of anticholinergic side-effects./** Indication de la mianserine compte tenu de son absence d'effets anticholinergiques. Acta Psychiatrica Belgica (Brussels). 78(5):781-786, 1978.

The clinical indications are discussed for the use of mianserin, a new tetracyclic antidepressant which has an effect similar to that of tricyclic compounds but without the undesired side-effects. The drug is particularly useful in the treatment of patients who do not react to other antidepressants or those who have stopped using them because of the side-effects. Mianserin may also be used with patients suffering from glaucoma, urinary or prostatic disorders, and cardiac problems, even when there has been a recent heart infarction. It is recommended for the aged, for patients in poor general health, and patients who are in a confused state following tricyclic antidepressant treatment. (Journal abstract modified)

002613 Carman, John Scott; Wyatt, Richard Jed. University Hospital, Department of Psychiatry, 619 19th St. S., Birmingham, AL 35294 **Use of calcitonin in psychotic agitation or mania.** Archives of General Psychiatry. 36(1):72-75, 1979.

The effects of increases in serum total calcium and inorganic phosphorus levels and decreases in cerebrospinal fluid (CSF) calcium level previously seen during periodic psychotic agitation or mania were studied. Synthetic salmon calcitonin was administered subcutaneously to 12 inpatients with several primary psychotic diagnoses in a double-blind placebo controlled trial. Calcitonin, which decreased serum calcium and phosphorus levels and increased CSF calcium level, appeared to produce transient (24 hour) increases in depression and decreases in arousal. Quantitative activity monitoring confirmed the rater's impression that this agent had tranquilizing or depressant effects in such patients. When given in the evening, this polypeptide also appeared to delay sleep onset. A decreased hypocalcemic response to calcitonin was noted in the agitated patients, which might explain the increases in serum calcium level described at the switch. 17 references. (Author abstract modified)

002614 Coppen, Alec; Ghose, Karabi; Rao, Rama; Bailey, John; Peet, Malcolm. Medical Research Council Neuropsychiatry Laboratory, West Park Hospital, Epsom KT19 8PB Surrey, England **Mianserin and lithium in the prophylaxis of depression.** British Journal of Psychiatry (London). 133(September):206-210, 1978.

Outpatients (n=41) with a history of at least three attacks of depressive illness were randomly allocated to treatment on a double-blind basis for 1 year with either mianserin hydrochloride 20mg three times daily plus placebo lithium tablets, or to lithium tablets once daily plus placebo mianserin tablets. After 1 year, the dosage of mianserin was increased to 30mg t.d.s. for a further 6 months. All but three of the patients had previously been stabilized on prophylactic lithium therapy. Lithium was found to be significantly superior to mianserin in avoiding admission to hospital or ECT. The overall affective morbidity index, calculated from global rating, showed no significant difference between drugs, but the index of the mianserin group was higher in the second 6 months than in the first. The lithium group showed no such change. Lithium remains the choice for the prophylaxis of unipolar recurrent depressive illness. 10 references. (Author abstract)

002615 Corveleyn, Jozef; Goossens, Lut; Verstraeten, Danny. Universitaire Psychiatrische Kliniek "Salve Mater', Lovenjoel, Katholieke Universiteit Leuven, Belgium **/Goal attainment scaling with chronic psychotic patients within the framework of a pharmacological investigation./** Goal attainment scaling bij chronische psychotische patienten in het raam van een medicamenteus onderzoek. Maandblad voor de Geestelijke Volksgezondheid (Amsterdam). 33(4):262-275, 1978.

A new neuroleptic drug was tested with the aid of the Goal Attainment Scale (GAS) to provide a definite method of evaluating the results of the therapeutic intervention. Thirty-five chronic psychotic patients were investigated for the effect of a new neuroleptic drug. With the GAS an individualized evaluation criterium was set up. A therapeutic goal was determined, levels of success defined, and at the end of therapy, the level attained was determined. The GAS instrument and methods and results of this experiment are described. The GAS appears to have a limited significance in the evaluation of the effect of the new drugs. However, the therapeutic aspect of the GAS is considered important in that it can provide means to a more goal oriented treatment for the chronic patient. 12 references. (Journal abstract modified)

002616 Cutler, Neal R.; Heiser, Jon F. Heiser: Dept. of Psychiatry and Behavioral Sciences, University of Texas Medical Branch, Galveston, TX 77550 **The tricyclic antidepressants.** Journal of the American Medical Association. 240(21):2264-2266, 1978.

The questions of why an evaluation for depression is important to all patients, which depressed patients should be treated, how much of which drugs should be used, and when consultation should be sought are considered, and the tricyclic antidepressants are examined. Because only 9.4% of depressions are recognized at initial evaluation by primary physicians, the diagnosis of depression is important. It is estimated that 40% of a group of mixed depressions will resolve in a month without treatment, and 70% will resolve with the use of tricyclic antidepressants. Research on plasma levels of tricyclic antidepressants suggests new clinical strategies for adjusting dosages; neurochemical studies may provide an appropriate selection process for choosing a tricyclic antidepressant. 13 references. (Author abstract modified)

002617 Daly, Robert Michael. Department of Public Welfare, Harrisburg, PA 17120 **Lithium-responsive affective disorders:**

model comprehensive plan for treatment. New York State Journal of Medicine. 78(4):594-601, 1978.

A rational plan for the development and implementation of a comprehensive mental health system for lithium treatment of manic-depression is described. The disease entity and its natural history are defined. Because of the low toxic therapeutic ratio of the lithium salt in humans, precise diagnosis is required. Since the plan being described is a public delivery system, the diagnostic classification boundaries are made exceptionally clear for its general service use. These boundaries can be expanded for research design. Finally, on the basis of this data, its epidemiology and a model delivery system for a specific geographic area (New York City) and at-risk population incorporating technical, administrative, and economic factors are presented. 42 references. (Author abstract modified)

002618 Davis, Robert A.; Taylor, Michael Alan; Abrams, Richard. Department of Psychiatry, Long Island Jewish-Hillside Medical Center, Glen Oaks, NY **Body fluid lithium measurements: severity of illness and prediction of outcome.** Biological Psychiatry. 13(5):595-599, 1978.

Lithium ion was measured in saliva and serum 24 hr after a loading dose of lithium, and the amount of lithium excreted in the urine was recorded during the 24 hr test period. Previous work which indicates a correlation between serum and mixed saliva lithium levels is supported by the results. On a subsample of manic patients, no correlation could be found between lithium retention and clinical outcome, age of onset, or pretreatment severity of illness. It is reported that a confirmation was not possible of a prior report that the 24 hr postloading dose serum lithium level was a predictor of eventual therapeutic dosage. 19 references. (Author abstract)

002619 De Buck, R. Avenue de Pantheon 58, B-1080 Bruxelles, Belgium **/The place of mianserin among the antidepressants./** Place de la mianserine parmi les antidepresseurs. Acta Psychiatrica Belgica (Brussels). 78(5):841-854, 1978.

The pharmacological and antidepressant properties of mianserin, a tetracyclic piperazino-azepine compound, are described. The drug has no central anticholinergic effects, inhibits 5-hydroxytryptophane, does not affect the reuptake of amine transmitters as do the tricyclics, and increases noradrenaline turnover. Clinical trials indicate that mianserin induces a hypomania in some manic depressed patients; that it is superior to placebo in antidepressive effects; and that it is as effective as imipramine and amitriptyline. It simultaneously works on anxiety, psychomotor retardation, and suicidal tendencies (via sedative properties) and also improves sleep. The value is further enhanced by its safety, since it has no cardiotoxic effects and does not interact with coumarin type anticoagulants. It can therefore be given to patients with glaucoma or prostatic hypertrophy. 35 references. (Journal abstract modified)

002620 Dencker, S. J.; Johansson, R.; Lindberg, D. Department II, Lillhagen Hospital, S-422 03 Hisings Backa 3, Sweden **Plasma levels and clinical response to megadose fluphenazine enanthate in three manic psychotics.** Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 32(5):369-373, 1978.

The correlations between symptom reduction, side-effects, and plasma drug levels were investigated in three manic psychotics treated with megadoses of fluphenazine enanthate. During the course of 1 week, each patient received one megadose of between 250 and 750mg. Early and rapid symptom reduction was observed along with plasma fluphenazine 15 to 30 minutes after injection. Optimal plasma values occurred between 2 and 5 days after injection along with steady symptom reduction. However, severe side-effects influenced manic symptom ratings. The patients with the highest fluphenazine plasma levels did not demonstrate extrapyramidal side-effects. It is concluded that increased therapeutic effects without additional side-effects were obtained with megadose treatment of fluphenazine. 9 references. (Author abstract modified)

002621 Finnerty, Richard J.; Goldberg, Harold L.; Rickels, Karl. Outpatient Psychopharmacology Research Group, West-Ros-Park Mental Health Center, 26 Central Avenue, Hyde Park, MA 02136 **Doxepin versus imipramine in psychoneurotic depressed patients with sleep disturbance: a double-blind study.** Journal of Clinical Psychiatry. 39(12):852-856, 1978.

The effects of imipramine and doxepin were compared in a randomized double-blind study of 97 psychoneurotic depressed patients with sleep disturbance symptoms. Mean doses of 112.7mg/day for doxepin and 116.7mg/day for imipramine were administered for a mean period of 26 days. While both drugs proved effective, 24 of 27 analyses of covariance showed imipramine to be superior to doxepin. This superiority was statistically significant for the anxiety/depressed factor measured by the Hamilton Depression Scale and for the total score, general neurotic feeling factor, cognitive performance difficulty factor, and the anger/hostility cluster of the Lipman-Rickels Scale. Mild to moderate side-effects were prevalent to a comparable degree in both treatment groups. 12 references. (Author abstract modified)

002622 Garreau, G; Sechter, D. Centre Hospitalier Sainte-Anne, 1, rue Cabanis, F-75674 Paris Cedex 14, France **/Carpipramine in the course of psychoses./** La carpipramine au cours des psychoses. Encephale (Paris). 4(5, Supplement):569-576, 1978.

In a paper presented at the Conference on the Concept of Inhibition in Psychiatry, held in Monastir, Yugoslavia, October 1978, a survey of 131 psychotic subjects treated with carpipramine is reported, along with a review of Japanese, German, and French publications about this drug. It is shown that the most valuable results were obtained in hebephrenics and in depressed schizophrenics. Carpipramine has a definite disinhibitory action against motor retardation, lack of energy, psychomotor slowness, and blunting of the affect. At low doses, paranoid schizophrenics become worse, but the emerged delusional and anxious phenomena can be avoided by higher doses. The drug is shown to have two kinds of effects: antidelusional and disinhibitory. It is suggested that even if it does not seem to be a true antidepressant, carpipramine does prove useful in deficits of the psychomotor tone, which were resistant to antidepressant drugs. 48 references. (Journal abstract modified)

002623 Gelenberg, Alan J.; Klerman, Gerald L. Department of Psychiatry, Harvard Medical School, Boston, MA 02114 **Maintenance drug therapy in long-term treatment of depression.** In: Brady, J., Controversy in psychiatry. Philadelphia, W. B. Saunders, 1978. 1087 p. (p. 281-301).

Drug therapy in the long-term maintenance treatment of patients with recurrent depression is explored. Topics discussed include: prognosis in acute depression, recurrence, bipolar patients, unipolar patients, cronicity, maintenance therapy, lithium, antidepressants, tricyclic antidepressants, psychosocial factors in recurrent depression, psychosocial status of the patient, and the therapeutic alliance. Recommendations for treatment of the bipolar, unipolar, other nonbipolar depressed patients and schizoaffective patients; and adverse effected are identified for lithium treatment. 51 references.

002624 Gladkova, K. I.; Ostroumova, L. I. Kafedra psikhiatrii Kubanskogo meditsinskogo instituta imeni Krasnoy Armii, Kuba, USSR **/Specific traits of clinical and social adaptation of**

patients with depressions in old age./ Osobennosti klinicheskoy i sotsial'noy adaptatsii bol'nykh s depressiyami pozdnego vozrasta. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 78(6):863-866, 1978.

Ninety-two elderly mental patients with involutional depressions were observed in order to determine their abilities for social adaptation. In 46 of the cases it was established that the level of social adaptation correlated with the patient's emotional response during psychopharmacological treatment sessions. In these cases, the positive response during extended treatment was accompanied by a gradual alleviation of the pathological disturbance, with an eventual transition to a pseudoneurotic level. This resulted in significant improvement of adaptational ability. In only five of the cases was there a marked decrease in adaptability despite the drug treatment. This occurred against a background of a stereotyped frozen melancholic state. 11 references. (Journal abstract modified)

002625 Gold, Philip W.; Goodwin, Frederick K.; Reus, Victor I. Clinical Psychobiology Branch, National Institute of Mental Health, 9000 Rockville Pike, Building 10, Bethesda, MD 20014 **Vasopressin in affective illness.** Lancet (London). 1(8076):1233-1236, 1978.

Research on the vasopressin function and its effect in affective illnesses are reviewed. Animal studies reveal that vasopressin deficiency produces deficits of behavior which are reversed by vasopressin, and that well developed systems exist for the distribution of vasopressin throughout the central nervous system and provide the means by which vasopressin may regulate cells controlling behavioral or physiological processes. Among the processes which vasopressin can influence are several of significance in the symptom complex of affective illness, including alterations in memory, changes in pain sensitivity, synchronization of biological rhythms, the timing and quality of REM sleep, and the regulation of fluid and electrolyte balance. In addition, vasopressin is functionally linked to monoamine neurotransmitter systems and is altered by pharmacological agents which affect mood. Some of the pharmacological and clinical data suggest that vasopressin function is diminished in depression and augmented in mania. However, sometimes alterations in vasopressin may be detectable only during crucial periods of the manic-depressive cycle. The hypothesis that vasopressin plays a role in disorders of human behavior can now be directly tested by radioimmunoassays of vasopressin in cerebrospinal fluid and plasma and by the administration of specific vasopressin analogues and inhibitors. 41 references. (Author abstract modified)

002626 Goodwin, Frederick K.; Extein, Irl L.; Wehr, Thomas A. Clinical Psychobiology Branch, Intramural Research Program, National Institute of Mental Health, Bethesda, MD 20014 **Some recent advances in psychobiology and psychopharmacology of affective disorders.** In: Ayd, F., Mood disorders. Baltimore, Ayd Medical Communications, 1978. 266 p. (p. 22-43).

A paper read at the Tenth Annual Taylor Manor Hospital Scientific Symposium, held in Baltimore in April 1978, is presented. Recent advances in the biological basis of affective disorders are explored. Topics discussed include: the spectrum of conditions from an ordinary human emotion to a medical syndrome with fixed depressed mood and physiological symptoms, the recurrent nature of affective illness, the biological hypotheses, the monoamine neurotransmitter systems, electrolytes and membranes, neuroendocrine systems, the monoaminergic neuron, the synaptic transmission, reserpine, iproniazid, the connection between brain amine levels and depression, lithium, central monoaminergic function, the concept of subgrouping, studies of urinary 3-methoxy-4-hydroxyphenylglycol (MHPG) in depressed patients divided into unipolar and bipolar subgroups, cerebrospinal fluid (CSF) 5-hydroxy indoleacetic acid levels (5HIAA), probenecid, the balance between transmitter systems, the antidepressant actions of tricyclic drugs, amitriptyline and imipramine, the acute clinical response of a depressed patient to amphetamine, the euphoric effects of amphetamines blocked by lithium, and dopamine systems in affective disorders. Predictions are made on drug effects in depressed patients with low urinary MHPG and depressed patients who have low CSF 5HIAA. 43 references.

002627 Guyotat, J. 11, quai General-Sarrail, F-69006 Lyon, France **/Inhibition and antidepressants./** Inhibitions et antidepresseurs. Encephale (Paris). 4(5, Supplement):533-539, 1978.

In a paper presented at the Conference on the Concept of Inhibition in Psychiatry, held in Monastir, Yugoslavia, October 1978, inhibition as a symptom is distinguished from inhibition as a process in three situations, including 1) antidepressants and melancholic inhibition, 2) antidepressants and chronic psychoses, and 3) neurotic depression. The action on inhibition is studied referring to the Kielholz classification of antidepressants. The risk of suicide by supressing inhibition is noted. The effects of antidepressants and stimulating neuroleptics are compared, and it is suggested that with the two types of psychotropic drugs, a disinhibitory effect can be obtained, but that antidepressants can better be used in paranoid personalities, loss of ego boundaries, and some schizophrenic-like syndromes; neuroleptics seem to be more disinhibitory in hebephrenics. The depressive core in these psychotic personalities is stressed. Cases with reinforcement of inhibition as a negative therapeutic reaction by antidepressants are described. 5 refernces. (Journal abstract modified)

002628 Hoc, J. Avenue de la Vecquee 52B, B-5000 Namur, Belgium **/Double-blind clinical study of mianserin and nortriptyline./** Etude clinique comparative en double insu de la mianserine et de la nortriptyline. Acta Psychiatrica Belgica (Brussels). 78(5):833-840, 1978.

The comparative effectiveness of mianserin and nortriptyline treatment on 36 depressed patients with a minimal score of 15 on the Hamilton rating scale was assessed over a 6 week period. Seventeen Ss received mianserin and 19 received nortriptyline. Therapeutic efficacy was similar for both drugs, without significant differences in time of action or duration of activity over the 6 week period. The number of side-effects was greater for nortriptyline, with a significant difference particularly noted in frequency and severity of tachycardia, dry mouth, and edema. (Journal abstract modified)

002629 Hollister, Leo E. Department of Medicine Veterans Administration Hospital, Palo Alto, CA 94304 **Tricyclic antidepressants (second of two parts).** New England Journal of Medicine. 299(21):1168-1172, 1978.

Clinical use of tricyclic antidepressants is reviewed. While interpatient variability to these drugs is axiomatic and doses may range from 50mg to 600mg daily, a daily dose of 150mg is a reasonable treatment goal for most patients. A single daily dose is recommended, and improvement should be apparent within 2 to 3 weeks of treatment with adequate doses. In refractory patients the possibility of drug induced, illness induced, or situational depression should be considered. Bipolar affective disorder and schizophrenia should also be ruled out. Tricyclics appear to be most effective in the treatment of endogenous depression. Where suicide is a possibility, electroconvulsive therapy should be considered. Combinations of drugs should be used with care. In general, side-effects are minor, but careful and conservative use is indicated in elderly patients and those with heart disease. Most drug reactions are pharmacodynamic: that with alcohol is

most common and of most importance. Overdoses present serious medical emergencies and require expert medical management. Precautions may be taken to prevent self-poisonings. 19 references.

002630 Izquierdo de la Torre, J.A. Departamento de Psiquiatria Y Psicologia, Facultad de Medicina, Universidad de Salamanca, Salamanca, Spain **/Maintenance treatment with lithium./** Tratamiento de mantenimiento con litio. Actas Luso-Espanolas de Neurologia, Psiquiatria, etc. (Madrid). 5(6):311-326, 1977.

Research on lithium's prophylactic use is surveyed and the most important experiments and the criticisms made against them are reviewed. The evolution of experimentation is divided into six periods beginning in 1958. The debate which has arisen oven the proper term to describe lithium's therapeutic effect is noted. Those specialists who opposed the term prophylactic as imprecise proposed such alternative terms as stabilizer, compensator, regulator, and equilibrator. Evaluation of experimental results has also caused debate. The problem of classifying the affective disorders and their natural evolution is mentioned. Clinical indications of lithium maintenance treatments and their relative efficacy are discussed, and practical patterns for a correct clinical use of the substance are established. Absolute and relative incompatibilities of substances; appropriate dosage and chemical control patterns; and specific problems of the doctor-patient relationship are described. 61 references. (Journal abstract modified)

002631 Janowsky, David; Judd, Lewis; Huey, Leighton; Roitman, Norton; Parker, Donal; Segal, David. Research Service, San Diego Veterans Administration Hospital, San Diego, CA **Naloxone effects on manic symptoms and growth-hormone levels.** Lancet (London). 2(8084):320, 1978.

The hypothesized link between endorphins and manic symptoms was investigated by administering naloxone to 12 patients (11 males, one female) with manic or hypomanic symptoms. When compared with placebo, naloxone caused small but significant mean decreases in both the Beigel-Murphy euphoria/grandiosity and the arousal/activation subscale scores. Although growth hormone concentrations rose after naloxone infusion, this effect was not statistically significant. However, frequently, the patients with the largest increases in serum growth hormone showed the greatest decreases in the sum of the subscale scores. 7 references.

002632 Kocsis, James H.; Lieberman, Kenneth W.; Reding, Georges R.; Stokes, Peter E. Department of Psychiatry, Payne Whitney Psychiatric Clinic, New York Hosp., Cornell Med. Center, New York, NY **High dose lithium therapy.** Biological Psychiatry. 13(6):759-762, 1978.

A manic patient is described who on two occasions showed blood lithium levels much higher than those ordinarily recommended, but with minimal toxic signs and with symptomatic improvement. The patient had been in a manic state characterized by motor hyperactivity, euphoria, religious and sexual preoccupations, distractability, and flight of ideas. Lithium chloride was begun at doses of .5meq/kg per day and gradually raised until mild toxic symptoms appeared at plasma lithium levels ranging from 1.18 to 2.34meq/liter. Fluphenazine was also administered for 10 days, possibly accounting for some of the clinical improvement seen. Plasma and red blood cell (RBC) lithium concentrations and 24 hour lithium urinary excretion were monitored daily. Mean RBC/plasma lithium concentration was .77. Physicians should recognize the possibility that manic patients who have not improved under lithium at 0.8-1.4meq/l plasma levels might respond favorably to higher doses at higher plasma levels than usually recommended. 10 references.

002633 Krishna, N. Rama; Taylor, Michael Alan; Abrams, Richard. Dept. of Psychiatry and Behavioral Sciences, University of Health Sciences, Chicago Medical School, Bldg. 50, North Chicago, IL 60064 **Response to lithium carbonate.** Biological Psychiatry. 13(5):601-606, 1978.

To determine response to lithium carbonate, the clinical and research records of 29 acutely ill hospitalized patients with affective disorder who received only lithium carbonate during their 1st week of treatment were examined. Nineteen group 1 patients could be continued on lithium ion alone, while 10 group 2 patients were significantly younger at illness onset, more severely ill on admission, clinically more colorful in dress and behavior, stayed more than twice as long in the hospital, and had more than twice the morbidity risk for affective disorder in first degree relatives. At discharge, both groups were equally improved, and 70% of group 2 patients were receiving lithium alone. Group 2 patients had a more severe or penetrant form of illness than group 1 patients, requiring neuroleptic drugs or ECT in addition to lithium therapy. However, it is reported that eventually they had a satisfactory outcome, suggesting therapeutic optimism and tenacity even in those patients who initially fail lithium alone and require polytreatment. 5 references. (Author abstract modified)

002634 Kuhne, Gert-Eberhard; Grunes, Jorn-Uwe; Knorr, Wolfgang; Perina, Lilith; Richter, Herbert; Rommel, Uta; Sorger, Reiner; Stock, Horst; Waldow, Norbert. Medizinische Akademie Magdeburg, Leipziger Strasse 44, DDR-301 Magdeburg, German Democratic Republic **/On the differential indications of desipramine: results of a controlled multi clinical study./** Zur Differentialindikation von Desipramin: Ergebnisse einer kontrollierten multiklinischen Studie. Psychiatrie, Neurologie und Medizinische Psychologie (Leipzig). 30(2):104-115, 1978.

The antidepressants desipramine and imipramine were compared in a controlled clinical experiment. A time differential remission of affective symptoms was discovered but was not initially detectable. The tachythymoleptic action of desipramine is discussed in reference to these results. Evaluation of the possibility of controlling affective dynamics shows different ranges of activity of desipramine and imipramine, with desipramine influencing negative psychoenergetic symptoms in the area of drives and emotions, while imipramine affects restrictive symptoms in addition to differential phenomena of psychomotor expression. 22 references. (Journal abstract)

002635 Kupfer, David J.; Hanin, Israel; Spiker, Duane; Neil, John; Coble, Patricia; Grau, Thomas; Nevar, Chris. Department of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261 **Amitriptyline plasma levels and clinical response in primary depression: II.** Communications in Psychopharmacology (Oxford). 2(5):441-450, 1978.

At the Symposium on Plasma Level Monitoring of Tricyclic Antidepressants held in Vienna in July 1978, the relationship between plasma levels of amitriptyline and clinical response in patients with primary depression was studied. Twenty-five patients with primary depression entered a double-blind protocol (amitriptyline or placebo) and their clinical status was determined by raters blind to the drug type, its dosage, and plasma levels (amitriptyline and nortriptyline). Plasma levels were assayed twice weekly by gas chromatography mass spectrometry. A negative correlation between the Hamilton Rating Scale and the plasma level of the two drugs was found at the end of the treatment period. When the group was divided into clinical responders and nonresponders the mean plasma levels of the two drugs discriminated the two groups by day 5 on 100mg/day, as well as at the end of the protocol. Due to the gradual stepwise increase of

the dosage schedule, conclusions can only be based on plasma, steady-state levels achieved for the last 7 to 10 days. Results add to the increasing evidence of a positive correlation between plasma levels and clinical improvement in patients with primary depression. Factors such as age, or clinical subtype such as psychotic/nonpsychotic, did not appear to exert a major influence on the results. 17 references. (Author abstract modified)

002636 Lion, John R. 645 Redwood Street, Baltimore, MD 21201 **Benzodiazepines in the treatment of aggressive patients.** Journal of Clinical Psychiatry. 40(2):70-71, 1979.

A double-blind controlled clinical trial of chlordiazepoxide, oxazepam, and placebo was conducted in 65 outpatients with past histories of temper outbursts, assaultive behavior, and impulsiveness associated with anxiety, hostility, and irritability. Of those tests showing statistically significant results, there was a tendency for oxazepam to be somewhat more effective in the reduction of anxiety than chlordiazepoxide. Oxazepam was also superior to the latter on one subscale of tests used to measure hostility. No paradoxical rage responses were noted. 11 references. (Author abstract)

002637 Lyons, H. A.; Degerli, M. Purdysburn Hospital, Belfast, Northern Ireland **Indications for the use of tranylcypromine and trifluoperazine (Parstelin).** Scottish Medical Journal (Glasgow). 23(4):307-309, 1978.

Thirty-two patients who were treated with a combination of tranylcypromine and trifluoperazine (Parstelin) are described. The patients were of three clinical groups: endogenous depression (7 patients), neurotic depressive reaction (10 patients), and phobic anxiety with some depressive features (15 patients). Satisfactory response was found in 10 out of the 15 patients with phobic symptoms, the response in the other two groups was not significant. Side-effects were troublesome in th neurotic depressive reaction group. In the phobic group the symptoms of the patients who responded were inclined to recur when the treatment was discontinued. It is suggested that the preparation may prove useful in the treatment of some phobic patients, but it is likely that the patients will have to remain on the drug for long periods of time. 26 references. (Author abstract modified)

002638 Majczak, Adam; Wielosz, Marian; Grzywa, Anna; Kornacki, Lech; Nagay, Jerzy; Jasinska, Maria. Klinika Psychiatryczna Instytutu Chorob Ukladu Nerwowego AM, ul. Abramowicka 2, 20-442 Lublin, Poland /**Clinical evaluation of oral penfluridol -- a neuroleptic with prolonged action in the treatment of schizophrenic psychoses.**/ Kliniczna ocena penfluridolu -- doustnego neuroleptyku o przedluzonym dzialaniu w leczeniu psychoz schizofrenicznych. Psychiatria Polska (Warszawa). 12(5-6):555-562, 1978.

A clinical evaluation of oral penfluridol, a neuroleptic with prolonged action in the treatment of schizophrenic psychosis, is presented. Penfluridol was used in 27 patients (11 women and 16 men) hospitalized at the psychiatric department in 1977. Most of the 22 patients were less than 30 years of age. In the acute phase of the illness they received short-acting neuroleptics, usually haloperidol, whereafter treatment was continued with penfluridol for 32 weeks. The mental state of the patients and the intensity of side-effects was evaluated every 4 weeks using Overall's scale for evaluation of psychopathological symptoms, Wing's behaviour scale, modified by Majczak, and a scale for the evaluation of side-effects. Very good or good improvement was obtained in 14 patients (51.9%) while 4 patients (14.8%) interrupted treatment after 28 weeks because of intensification of psychopathological symptoms. The mean dosage of the drug in the first 4 weeks and after 32 weeks of administration amounted to 32mg and 29mg a week, respectively. Not very intense mental side-effects occurred in 11 patients, while side-effects originating from the extrapyramidal or vegetative systems occurred in 6 and 5 patients, respectively. Effects obtained showed penfluridol to be well tolerated and suited for outpatient treatment owing to the facility of use and the insignificant number of side-effects. It activates the patients, improves their contact with the physician, and promotes readaptation to the environment. 11 references. (Journal abstract modified)

002639 Montgomery, S. A.; Montgomery, D. B.; McAuley, R.; Rani, S. J. Academic Department of Psychiatry, Guy's Hospital Medical School, London SE 1, England **Mianserin plasma levels and differential clinical response in endogenous and reactive depression.** Acta Psychiatrica Belgica (Brussels). 78(5):798-812, 1978.

Fifty patients with moderate to severe primary depression were treated in equal groups of inpatients and outpatients with a constant dose of 60mg mianserin daily for 4 weeks in a double-blind placebo controlled trial. Dosage was either three times daily or once nightly, and no difference in apparent compliance, side-effects, or therapeutic effectiveness occurred on the two regimens. Patients with endogenous depression had a significant negative correlation between plasma levels of mianserin and therapeutic response on the Hamilton Rating Scale or on the new scale developed by Montgomery and Asberg. There was a significant correlation between drug plasma levels and age in endogenous depression. In patients with reactive depression, no significant relationship occurred between plasma levels and therapeutic response or with age. Findings support the hypothesis that the relationship between mianserin plasma level and clinical response is more likely to be demonstrated in endogenous depression. 32 references. (Journal abstract modified)

002640 Muskin, Philip R.; Rifkin, Arthur. no address **Tricyclic antidepressants in the treatment of depression in conjugal bereavement.** Archives of the Foundation of Thanatology. 7(1):10, 1978.

In a summary of a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, a review of several authors' work on the symptomatology of grief during the acute stages and the first year of bereavement was presented. Several features commonly observed during mourning that are identical with the diagnostic criteria for affective illness were noted. A large subgroup of bereaved family members emerges at 1 month following a death within the family who meet research criteria for depression, many of whom are still depressed 1 year later. A redefinition of grief and pathological grief was suggested on the basis of drug responsivity. Research currently in progress to treat widows who meet stringent criteria for depression with imipramine was discussed. The need for further study was emphasized in light of the high mortality rate in the conjugally bereaved.

002641 no author. no address **Tricyclic antidepressant concentrations and clinical response.** British Medical Journal (London). 2(6140):783-784, 1978.

Recent research into the association between nortriptyline concentrations and clinical response are reviewed. Previous studies of this association have been mixed and inconclusive. A recent study by Montgomery et al (1978) suggests that plasma nortriptyline concentrations in an intermediate range (above 50 mcg/1 and below 200 mcg/1 are related to clinical response. Further, it was found that nortriptyline mean plasma clearance in the depressed sample was only about half that of normals, and that a single estimation of plasma nortriptyline 48 hours after a test dose will accurately predict eventual steady state

concentrations and can be used to adjust the clinical dose. It is suggested that the lack of consistency in the literature may be due to technical problems with estimating drug concentrations, different ways of evaluating types of patients and clinical response, and further pharmacokinetic factors. It is suggested that monitoring plasma concentrations to predict correct dosage might increase the efficacy of nortriptyline and other tricyclics. 17 references.

002642 Okamoto, Kenichiro; Nakano, Tetsuo; Inanaga, Kazutoyo. Department of Neuropsychiatry, Kurume University School of Medicine, 67 Asahi-machi, Kurume 830, Japan **Clinical experience with Org GB94 (Mianserin hydrochloride), a new tetracyclic antidepressant.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 32(2):171-183, 1978.

A total of 21 depressed patients (nine had endogenous depression, five had involutional or senile depression, five had neurotic depression, and two had depression due to other diseases) were given Org GB94 (Mianserin hydrochloride), a new tetracyclic antidepressant, in a 4 week clinical trial. The onset of effect of Org GB94 is rapid: a response to the treatment was observed in 2.7days. An antidepressant activity comparable to that of existing antidepressants was found, and the data show that Org GB94 was very effective in endogenous, involutional, and senile depression. Results indicate that symptoms such as depressed mood, anxiety and retardation, and suicidal thought are among the first to improve. Anticholinergic side-effects were extremely rare and other untoward effects were mild in nature. 15 references.

002643 Olsen, Edwin J.; Bank, Lew; Jarvik, Lissy F. Veterans Administration Hospital, Brentwood, Los Angeles, CA 90073 **Gerovital-H3: a clinical trial as an antidepressant.** Journal of Gerontology. 33(4):514-520, 1978.

A clinical trial of gerovital-H3 as an antidepressand with an elderly sample is reported. Twenty-five volunteers, all in their fifth decade or beyond, all with mild or moderate, nonpsychotic depression of at least several months' duration participated in a double-blind study of gerovital vs. placebo. There was no significant difference between the gerovital and placebo groups; both groups showed significant improvement on self-rating as well as observer rating scales. 20 references. (Author abstract modified)

002644 Ostrow, David G.; Pandey, Gyanshyam N.; Davis, John M.; Hurt, Stephen W.; Tosteson, Daniel C. Institute for Psychosomatic and Psychiatric Research, Michael Reese Medical Center, 2959 South Ellis Ave., Chicago, IL 60616 **A heritable disorder of lithium transport in erythrocytes of a subpopulation of manic-depressive patients.** American Journal of Psychiatry. 135(9):1070-1078, 1978.

In a revised version of a paper presented at the 130th Annual Meeting of the American Psychiatric Association, held in Toronto, Ontario, May 1977, the lithium transport in patients with affective disorders and normal individuals was investigated. The determination of the in vivo erythrocytes/plasma Li ratio is determined by the equilibrium between Li influx (ouabain sensitive Na-K pump and ouabain insensitive leakage pathways) and Li efflux (phloretin sensitive Li-Na counterflow). It was found that a deficiency of Li-Na counterflow was responsible for the high in vivo ratio observed in a manic patient. This defect was related to an alteration in the membrane Na exchange system and was under genetic control. The level of counterflow before lithium therapy was found to be an excellent predictor of the in vivo Li ratio and was deficient in approximately one fourth of manic-depressive patients but not in controls, schizophrenics, or unipolar depressed patients. 34 references. (Author abstract modified)

002645 Philipp, M.; Marneros, A. Psychiatrische Universitatsklinik, Langenbeckstrasse 1, D-6500 Mainz, Germany **Chronobiology and its implications for pharmacotherapy of endogenous depression.** Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 11(5):235-240, 1978.

A clear circadian rhythm in the therapeutic effect of single doses of lofepramine was demonstrated in a study of 30 inpatients with endogenous depression. Patients treated with lofepramine at 12p.m. had significantly lower depression scores than patients treated at 8a.m. or 4p.m. In a second study, patients treated with a single dose of 210mg lofepramine at 12p.m. showed significantly greater response to treatment than did patients treated on the conventional divided dose schedule (70mg lofepramine three times a day). The implications of these chronopharmacological findings for treatment with thymoleptic drugs are discussed. 60 references. (Author abstract modified)

002646 Poldinger, W.; Gammel, G. Kantonale Psychiatrische Klinik, CH-9500 Wil, Switzerland **Differences in effect between nomifensine and nortriptyline.** International Pharmacopsychiatry (Basel). 13(1):58-68, 1978.

The effects of nomifensine and nortriptyline were investigated in a double-blind study on outpatients with retarded depression. A group of 40 patients (17 males and 23 females) with endogenous, endogenous/psychogenic, or psychogenic depression were divided into two treatment groups. Over 21 days, all patients were given three 50mg capsules of nomifensine or nortriptyline per day. With the aid of a depression scale, a significant improvement in the psychic symptoms was noted in both groups. There was no evidence of a significant difference in the two drugs, although the data obtained from dropouts suggest that nomifensine had a better effect. It is concluded that nomifensine is suitable for treating patients with retarded depressions. (Author abstract modified)

002647 Poling, Alan; Appel, James B.; Ryan, Charlotte. University of South Carolina, Columbia, SC 29208 **Behavioral pharmacology and the use of psychotropic agents in terminal illness.** Archives of the Foundation of Thanatology. 7(1):29, 1978.

In a summary of a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, the use of the observational techniques of the behavioral scientist in the development of a clinically useful pharmacology of terminal illness was proposed. Time sampling techniques involving multiple observers would allow quantification of certain important behaviors, for example, positive and negative verbalizations about death, and would provide an index of the reliability with which these behaviors were measured. In addition, behavioral pharmacologists have gained appreciable knowledge of the reinforcing, conditioned, and discriminitive stimulus properties of many compounds. These different effects may occasionally benefit certain patients. It is concluded that behavioral pharmacology may help to study the effects of psychotropic agents on dying patients empirically.

002648 Poole, A. J.; James, H. D.; Hughes, W. C. Moorhaven Hospital, Bittaford, Ivybridge, South Devon, England **Treatment experiences in the lithium clinic at St. Thomas' Hospital.** Journal of the Royal Society of Medicine (London). 71(12):890-894, 1978.

The utility of lithium carbonate given in quantity as an agent in the prevention of recurrent bipolar affective, unipolar manic,

or unipolar depressive states was investigated. Lithium carbonate is a useful agent in the prophylaxis of recurrent affective disorders in the psychotic (unipolar or bipolar) as opposed to the neurotic, personality disordered, or schizoaffective groups. A good outcome is related to a positive family history of affective disorder, and to the absence of precipitating causes for illness episodes. The importance of serum lithium measurement is confirmed, but it is suggested that a prophylactic serum level range could be 0.5-0.9mmol/1. Caution is recommended in the treatment of the elderly by this means because of the increased incidence of unwanted effects. 20 references. (Author abstract modified)

002649 Prakash, Rudra; Sethi, N.; Sethi, B. B. Department of Psychiatry, King George's Medical College, Lucknow, India **Lithium in affective disorders.** Indian Journal of Psychiatry (Poona). 20(4):380-383, 1978.

The effects of lithiumn carbonate on the prophylaxis of primary affective disorders were examined with 22 patients. Only two subjects were categorized as nonresponders by evaluatory criteria while the remainder of the patients showed varying degrees of prophylactic response. Median effective dose of lithium as required by responders was 750mg/day. It was found that the two nonresponders were classified as rapid cyclers, an observation which is consistent with other studies. It is concluded that lithium is endowed with a great prophylactic potential for the long-term management of patients with primary affective disorders. 15 references. (Author abstract modified)

002650 Pull, C. B.; Pichot, P.; Dreyfus, J. F. Clinique de la Faculte, Rue de la Sante 100, F-75014 Paris, France **/A double-blind comparison between mianserin and imipramine./** Une compariaison, en double insu, entre mianserine et imipramine. Acta Psychiatrica Belgica (Brussels). 78(5):827-832, 1978.

A group of 54 depressed patients aged 18 to 65 years were treated for 4 weeks with a daily dose of either 60mg mianserin or 150mg imipramine in a double-blind controlled trial. Results obtained from the Hamilton and Beck depression inventories, the Brief Psychiatric Rating Scale, and on a global rating scale indicated no significant differences in the efficacy of the two drugs. The frequency of side-effects was significantly lower in the mianserin group. (Journal abstract modified)

002651 Rao, A. Venkoba; Hariharasubramanian, N. Dept. of Psychiatry, Madurai Medical College, Madurai, India **Lithium treatment of affective disorders -- certain observations.** Indian Journal of Psychiatry (Poona). 20(4):304-309, 1978.

The effects of lithium in prophylaxis and in the therapy of affective disorders was examined in 37 patients with manic depressive psychosis. Observations were made of the patients' attendance at a lithium clinic over a period of a year and a half. The patients (excluding one with a 48 hour psychosis) fell into three groups according to an analysis of their response to lithium. The good responders achieved complete remission in 30 to 60 days of treatment and maintained euthymia. The moderate responders also remitted but suffered relapse. The poor responders failed to achieve remission and persisted with symptoms which were markedly hypochondriacal and schizo-affective. Several factors which influenced response to lithium are discussed. 20 references.

002652 Rapoport, Judith L. Unit on Childhood Mental Illness, National Institute of Mental Health, Bethesda, MD 20014 **Antidepressant drug use in child psychiatry.** In: Ayd, F., Mood disorders. Baltimore, Ayd Medical Communications, 1978. 266 p. (p. 44-66).

A paper read at the Tenth Annual Taylor Manor Hospital Scientific Symposium, held in Baltimore in April 1978, is presented. Current concepts of drug treatment of childhood depression are reviewed, and caution is urged in employing the diagnosis of depression in young patients before they reach puberty. Topics discussed include: definitions and validation of the concept of childhood depression, drug treatment, anxiety, enuresis, hyperactivity, stimulant drugs and mood, monoamine oxidase inhibitors, lithium, and the strategy of examining the behavioral effects of drugs known to alter mood in adults. It is argued that the weight of clinical evidence shows that childhood depressive disorder is rare, but that it can occur. The rarity may provide an important approach to the biology of affective disorder. It is suggested that before puberty, some difference in physiological status, such as immaturity of neurotransmitter systems, or a difference in receptor sensitivity, provides protection against drastic and sustained mood alteration unless the most dire conditions are present. 79 references.

002653 Risch, Samuel C.; Huey, Leighton Y.; Janowsky, David S. Department of Psychiatry, San Diego VA Hospital, 3350 La Jolla Village Drive, La Jolla, CA 92161 **Plasma levels of tricyclic antidepressants and clinical efficacy: review of the literature -- Part II.** Journal of Clinical Psychiatry. 40(2):58-69, 1979.

The literature regarding the relationship between plasma levels of the various tricyclic antidepressants and their clinical efficacy is reviewed. Where available, drug/drug interactions, pharmacokinetics, and other factors influencing tricyclic plasma levels are discussed. Evidence suggests a curvilinear relationship between nortriptylene plasma levels and efficacy, and a linear relationship between plasma levels of imipramine plus demethylimipramine and clinical response in endogenously depressed patients. A significant, but less clear relationship had been found between amitriptyline plus nortriptyline plasma levels and efficacy. Further elucidation is required for protriptyline, desmethylimipramine, doxepin, clomipramine, maprotiline, and butriptyline. Statistical problems and methodological limitations of these studies are examined, and directions for future research are suggested. 120 references.

002654 Schatzberg, Alan F. McLean Hospital, 115 Mill St., Belmont, MA 02178 **Benzodiazepines in depressive disorders: a clinical guide.** Southern Medical Journal. 71(2):18-22, 1978.

Double-blind studies comparing benzodiazepines with tricyclics in the treatment of depression were reviewed in a paper presented at the McLean Hospital Symposium held in Dallas, November 1977. It is suggested that depressed patients should be categorized into endogenous and nonendogenous groups. For endogenous patients, tricyclics are clearly preferable to benzodiazepines. Benzodiazepines may have limited short-term use for sedation. For endogenous disorders, tricyclics tend to be more effective with benzodiazepines as an alternative for reducing certain symptoms and in patients who cannot tolerate tricyclic side-effects. For patients who have a mixed endogenous/nonendogenous depression, it is suggested that a tricyclic should be considered as primary treatment and a benzodiazepine as secondary treatment. 55 references.

002655 Schatzberg, Alan F. McLean Hospital, Belmont, MA **The psychopharmacology of depression: using the biogenic amine hypothesis to treat depressed patients.** Behavioral Medicine. 5(11):49-50, 52-54, 1978.

Clinical implications of biogenic amine research in affective disorders are examined. Research focusing on norepinephrine, serotonin, and 3-methoxy-4-hydroxy-phenylglycol (MHPG) in depression is reviewed. Psychopharmacological studies have indicated the existence of two types of edogenous unipolar de-

pressive disorder: one characterized by low MHPG and responsive to imipramine, the other characterized by high MHPG and responsive to amitriptyline. Although a number of variables may affect MHPG excretion, clinical application of MHPG excretion analysis should be of use in determining antidepressant regimens. Additional research has suggested that bipolar depressives are distinguishable from other disordered patients on the basis of catecholamine metabolite profiles. Drug pharmacokinetics, and determination of dosage/response levels are also discussed. 11 references.

002656 Sencicle, Lorraine. no address **/Rescue of a 28-year-old suicidal housewife./** Jean's taken an overdose. Nursing Mirrow (London). 147(23):58-60, 1978.

An anecdotal case report is presented which outlines the efforts made by the community psychiatric nursing service, the general practitioner, the consultant psychiatrist, and the housing welfare officer in helping a 28-year-old suicidal housewife resolve her problems. Following a period of depression and preoccupation, the patient appeared happier and more adjusted in the days preceding her suicide attempt. On discharge, the psychiatric consultant, fearing further attempts, recommended a visit to the patient's home by the community psychiatric nurse. Discussion with the patient revealed a variety of family, financial, and emotional problems. Despite the recommendations of the nurse and the psychiatrist that the patient be rehospitalized, both the patient and her family remained adamantly opposed to a readmission. Imipramine therapy was initiated. The family members aided in running the household, and appropriate referrals resulted in the family being able to move into a less expensive and more pleasant apartment. The patient appears to have made a successful recovery.

002657 Shoda, Hideshi. Shinshu University, Japan **Continuative changes of cyclic AMP in manic depressive psychosis: on the correlation of lithium carbonate treatment.** Psychiatria et Neurologia Japonica (Tokyo). 80(7):383-404, 1978.

In a controlled study, eight manic-depressive patients were treated with lithium carbonate (600mg/day for 14 days) and their response to the treatment was correlated with body and serum lithium content and with 24 hour urinary excretion of cyclic AMP. Of the eight patients, three were classed as rapid responders, three delayed responders, and two as rapid cyclers. Both rapid and delayed responders had a high accumulation of lithium in the body. There was, however, no correlation between the change in the clinical picture and serum lithium content. With improvement in the clinical picture, neither delayed nor rapid responders showed any significant increase in urinary excretion of cyclic AMP. In the case of the two rapid cyclers, urinary cyclic AMP excretion tended to decrease in the depressive phase and increase in the manic phase. This tendency was not changed when lithium treatment was discontinued. 104 references.

002658 Smith, A. H. W.; Naylor, G. J. Department of Psychiatry, University of Dundee, Dundee, Scotland **The antidepressant properties of mianserin and its effect on sleep.** Acta Psychiatrica Belgica (Brussels). 78(5):813-826, 1978.

A group of 39 female patients who were diagnosed as manic-depressives or psychotic-depressive were treated with mianserin or placebo administrations. Night sleep time, the Beck Self-Rating Inventory (BSRI), and staff nurses' ratings were measured before and after treatment. Blood samples for estimation of mianserin levels were taken on day 14. On the BSRI, 5 of the 21 mianserin patients improved significantly, whereas the 18 placebo Ss showed no change. Some improvement in mean daily nurse ratings was noted for placebo Ss, but greater improvement occurred in the mianserin group, particularly toward the end of the 14 days. Sleep improved significantly in mianserin Ss. Blood levels did not significantly correlate with changes in mood or sleep. Improvements in sleep were probably due to the hypnotic sedative properties of the drug. The results confirm that mianserin is an antidepressant. (Journal abstract modified)

002659 Titeca, J. Avenue de l'Exposition 341, B-1090 Bruxelles, Belgium **/The place of psychopharmacology in the treatment of depressions./** La place de la psychopharmacologie dans le traitement des depressions. Acta Psychiatrica Belgica (Brussels). 78(5):746-755, 1978.

The role of psychopharmacology in the treatment of depression is examined, emphasizing that great progress in the field over recent years and the refinement of numerous psychotherapeutic techniques has provided the psychiatrist with effective means for treating and curing affective disorders. In certain cases, however, electroconvulsive shock therapy performed under anesthesia and under cover of a myoplegic still remains necessary. This option should always be considered with depressed patients and it is not necessarily harmful to the patient.

002660 van Kammen, Daniel P.; Murphy, Dennis L. National Institute of Mental Health, Bldg. 10, Rm. 4N214, 9000 Rockville Pike, Bethesda, MD 20014 **Prediction of imipramine antidepressant response by a one-day d-amphetamine trial.** American Journal of Psychiatry. 135(10):1179-1184, 1978.

At the 129th annual meeting of the American Psychiatric Association held in Miami Beach, May 1976, a paper was presented which investigates the existence of an association between the acute activation, euphoria, and antidepressant responses to d-amphetamine and the antidepressant response to imipramine during a 4 week trial. Comparison of the resonses of 13 patients with a diagnosis of primary affective disorder to d-amphetamine on two different days during a double-blind trial indicate that differences in d-amphetamine response are consistent, replicable characteristics of individual depressed patients. The variables of sex, diagnosis, diurnal mood variation, platelet MAO activity, and MMPI scale scores were of minimal assistance in revealing factors that might be associated with activation or antidepressant responses to d-amphetamine in this small patient group. 36 references. (Journal abstract modified)

002661 Ziegler, V. E.; Wylie, L. T.; Biggs, John T. Department of Psychiatry, School of Medicine, Washington University, St. Louis, MO 63110 **Intrapatient variability of serial steady-state plasma tricyclic antidepressant concentrations.** Journal of Pharmaceutical Sciences. 67(4):554-555, 1978.

Serial steady-state plasma measurements of amitriptyline, desipramine, desmethyldoxepin, doxepin, imipramine, nortriptyline, or protriptyline were made in 23 patients undergoing drug treatment for depression. Each patient was monitored for compliance by pill counts, and sampling time was carefully controlled to determine intrapatient variability of steady-state tricyclic levels on a day to day basis. The coefficients of variation during serial sampling of the various drugs were: amitriptyline, 21%, desipramine, 26%; doxepin, 21%; imipramine, 14%; nortriptyline, 13%; and protriptyline, 17%. Since the therapeutic ranges for the tricyclic antidepressants are relatively wide, coefficients of variation of these magnitudes indicate that the position of an individual patient in relation to the optimal therapeutic range can be reliably determined on a clinical basis. 10 references. (Author abstract)

10 DRUG TRIALS IN NEUROSES

002662 Channabasavanna, S. M.; Jayram, S. S.; Kodandaram, P. National Institute of Mental Health and Neurosciences, Ban-

galore (560027), India **Clinical study of haloperidol and diazepam in anxiety states: a double blind trial.** Current Therapeutic Research. 24(4):381-387, 1978.

A study to assess the anxiolytic properties and relative safety of haloperidol and diazepam was conducted. In a double-blind trial, 95 patients suffering from anxiety were treated with either diazepam or haloperidol. The 80 patients completing 4 weeks of treatment were assessed subjectively and objectively by Hamilton rating scale. The results at the end of 2 weeks and 4 weeks of therapy showed that haloperidol is as effective as diazepam in controlling anxiety. The drugs were also found to be equally effective in both public and private settings. Differences were not statistically significant. The side-effects were minimal and rtansient for both groups, although the incidence of drowsiness in the diazepam treated group was higher. 12 references. (Author abstract modified)

002663 Cole, J. O. McLean Hospital, 115 Mill St., Belmont, MA 02178 **Drug treatment of anxiety.** Southern Medical Journal. 71(2):10-14, 1978.

Pharmacotherapy of anxiety in patients treated in nonpsychiatric medical practices was examined in a paper presented at the McLean Hospital Symposium held in Dallas, November 1977. Antianxiety drugs are divided into sedative hypnotics and autonomic sedatives, and side-effects such as oversedation, disinhibition, and physical dependence are discussed. Principles of therapy are outlined and predictors of improvement are provided. It is suggested that patients responding best to benzodiazepines generally present with relatively pure anxiety symptoms, have good preillness adjustment and health, wish drug therapy but realize they have emotional problems, and receive their therapy from a doctor who is comfortable both with the particular patient and with the drug he is prescribing. 21 references.

002664 Downing, Robert W.; Rickels, Karl. Rickels: 203 Piersol Building, University Hospital, 3400 Spruce Street, Philadelphia, PA 19104 **Prediction of response to chlordiazepoxide and placebo in anxious outpatients: an attempt at replication.** Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 11(5):207-219, 1978.

The stability of a set of nonspecific factors in predicting the response to chlordiazepoxide (CDZ) or placebo (PBO) was examined, using data from 447 primarily anxious neurotic outpatients treated with CDZ or PBO in 4 week, double blind drug trials performed over the past 10 years. Modest replicability and considerable drug specificity was found for the global improvement measure. Replicability was considerably higher for a patient measure of symptom change, but its specificity to treatment agent was considerably lower. 24 references. (Author abstract modified)

002665 Feldman, Lore. no address **Anxiety...panic! researchers are testing new treatments.** Emissary. 10(4):12, 1978.

A variety of treatments for anxiety are discussed. A phenothiazine, a minor tranquilizer, and relaxation training with biofeedback were compared to see which method works best. Prothiaden, an antidepressant widely used in England for anxious patients, but still an investigational drug in this country, was studied. Deconditioning with sodium lactate, which causes symptoms of anxiety, was compared with implosive therapy, a verbal psychotherapeutic method intended to wean the anxious patient away from his or her problem. Volunteers between the ages of 18 and 55 years old, with no health problems except disabling anxiety, are employed to serve as subjects for each study.

002666 Ives, John O.; Robinson, Donald S.; Nies, Alexander; Ravaris, C. Lewis; Korson, Lorraine B.; Lamborn, Kathleen R. Department of Psychiatry, University of Vermont College of Medicine, Burlington, VT 05401 **The ineffectiveness of chlordiazepoxide in depressive disorders.** Psychiatric Journal of the University of Ottawa (Ottawa). 3(2):115-119, 1978.

In studies which compared the antidepressant activity of phenelzine and placebo, 23 patients also received chlordiazepoxide in dosages frequently employed to treat depressive-anxiety states, whereas 52 patients did not. Improvement was similar for those patients who received chlordiazepoxide and for those who did not, in both the phenelzine and placebo treatment groups. These results suggest that chlordiazepoxide does not have significant usefulness in outpatients with depressive-anxiety syndromes. 31 references. (Author abstract)

002667 Peyrouzet, J. -M.; PeRier, M. 2, rue de Phalsbourg, F-75017 Paris, France **/Carpipramine in neuroses./** La carpipramine dans les nevroses. Encephale (Paris). 4(5, Supplement):577-585, 1978.

In a paper presented at a Conference on the Concept of Inhibition in Psychiatry, held in Monastir, Yugoslavia, October 1978, the limits of drug therapy in neuroses are outlined and rare literature is reviewed reporting on the indications of carpipramine in neurotic symptoms. Acting upon symptom patterns consisting essentially of asthenia, inhibition and psychomotor impairment, raising the level of activity, stimulating enthusiasm and related activity, carpipramine would appear to represent a new advance in the treatment of some neurotic symptoms, partially encompassing the borderline indications of antidepressants and those of certain disinhibitory neuroleptic agents. Three case studies of neurotic patients helped by carpipramine are provided. 33 references. (Journal abstract modified)

002668 Shusterman, Neil H. no address **Treatment of anxiety: phenobarbital versus the benzodiazepines.** Delaware Medical Journal. 50(11):605-607, 1978.

The benzodiazepines are compared with barbiturates in terms of efficacy, safety, compatibility with other drugs, and economy for the treatment of anxiety. At the present time there seems to be no hard evidence that benzodiazepines are more effective than barbiturates for the treatment of anxiety. The benzodiazepines have, however, been shown to be clearly more safe than the barbiturates. Both drugs have been shown to interact with specific anticonvulsant medications. When prescribed carefully, phenobarbital is an effective, economical drug that relieves anxiety rapidly, reliably, and with few side-effects. It is suggested that physicians should carefully review their habits, and think critically before prescribing benzodiazepines rather than significantly less expensive barbituarates. 9 references.

002669 Solomon, Kenneth; Hart, Ruth. Dept. of Psychiatry, Box 907 Medical College of Virginia, Richmond, VA 23298 **Pitfalls and prospects in clinical research on antianxiety drugs: benzodiazepines and placebo -- a research review.** Journal of Clinical Psychiatry. 39(11):823-831, 1978.

The research methodology of 78 double-blind studies comparing benzodiazepines and placebo in treating neurotic anxiety is critically reviewed. Many faults are noted in areas of subject selection assessment of response, study design and data analysis. Although 56.4% of the studies reviewed had results demonstrating a significant difference in clinical response between benzodiazepines and placebo, the frequent methodologic difficulties and inconsistent results from study to study lead to questions on the efficacy of these drugs as a treatment for anxiety. A need for better designed studies is discussed and some research methodologies proposed. 91 references. (Author abstract)

002670 Stern, R. S. Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 England **Obsessive thoughts: the problem of therapy.** British Journal of Psychiatry (London). 133(September):200-205, 1978.

Patients with obsessive thoughts were treated in two pilot studies: in the first patients were given thought stopping instructions, which were contrasted with relaxation therapy; in the second patients were treated by satiation (flooding) followed by thought stopping and a course of amitriptyline. Overall results were poor, but one type of obsessive thought (horror/disgust) did respond well to satiation, and it is thought that results justify separating this type of obsessive complaint from others for purposes of therapy. 17 references. (Author abstract modified)

002671 Walsh, B. Timothy; Katz, Jack L.; Levin, Joseph; Kream, Jacob; Fukushima, David K.; Hellman, Leon D.; Weiner, Herbert; Zumoff, Barnett. Department of Psychiatry, Montefiore Hospital and Medical Center, 111 East 210th Street, Bronx, NY 10467 **Adrenal activity in anorexia nervosa.** Psychosomatic Medicine. 40(6):499-506, 1978.

Adrenocortical activity was studied in 19 emaciated women with anorexia nervosa. Relative to body size, the patients' mean cortisol production rates were significantly elevated compared to those of age and sex matched normal controls. The 24 hour mean plasma cortisol concentration in 18 patients was significantly higher than that of the controls; and the average excretion of urinary free cortisol in 9 patients was significantly greater than that of the controls. Three patients underwent overnight suppression with 1mg of dexamethasone and had inadequate responses. These data suggest that cortisol production is excessive in emaciated patients with anorexia nervosa due to a disturbance of the hypothalamic pituitary mechanisms regulating adrenocortical function. The excessive adrenal activity may reflect certain psychobiological disturbances as well as the effects of malnutrition. 44 references. (Author abstract)

002672 Weir, James H. P.O. Box 377, Morris Plains, NJ 07950 **Prazepam in the treatment of anxiety: a placebo-controlled multicenter evaluation.** Journal of Clinical Psychiatry. 39(12):841-847, 1978.

A double-blind randomized multicenter parallel group comparison of prazepam in divided doses versus placebo was conducted by 15 investigators among 847 patients presenting with anxiety alone or concurrent with other medical illnesses. Study groups were well matched for age, sex, and level of pretreatment symtomatology. Efficacy evaluation by a physician questionnaire included serial assessment of global improvement plus 10 target signs/symptoms during the 2 to 4 weeks of treatment. Prazepam was statistically significantly superior to placebo as shown on final treatment scores for global improvement ratio and for target symptoms of anxiety, tension, irritability/hostility, depressive mood, insomnia, and somatization. 28 references. (Author abstract)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

002673 Belmaker, R. H.; Gagrat, D.; Hamilton, J. Ezrath Nashim Mental Hospital, Jerusalem, Israel **Acetylcholine and gamma-aminobutyric acid as mechanisms in the treatment of acute dystonia and akathisia.** Israel Journal of Medical Sciences (Jerusalem). 14(9):1003, 1978.

A summary of a paper read at the 41st Meeting of the Israel Physiological and Pharmacological Society held March 1978, in Jerusalem is presented. A double-blind randomized controlled study of diazepam, 5 mg i.v.,vs. diphenhydramine, 50 mg i.v.,in dystonia and akathisia was performed. Of 20 patients with dystonia, 10 received diazepam and 10, diphenhydramine. Of 20 with akathisia, 9 received diazepam and 11 diphenhydramine. Ratings at 5, 15, 30, and 120 min found marked and equal effectiveness for both treatments. It is concluded that the action of diazepam in dystonia and akathisia is probably central and may relate to GABA functioning in the basal ganglia. (Author abstract modified)

002674 Benjamin, David M. Dept. of Medical Research, Hoffmann-La Roche, Inc., Nutley, NJ **Problems of polypharmacy.** Archives of the Foundation of Thanatology. 7(1):11, 1978.

In a summary of a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, drug interactions involving psychopharmacologic or analgesic agents used by dying patients and bereaved family members were discussed. The treatment of a dying patient suffering from a chronic debilitating disease may include analgesic agents, antidepressants, and hypnotic drugs. Depressed or bereaved family members may receive psychotropic drugs to help control anxiety, depression, or insomnia. During this period of stress, both patient and family members may turn to alcohol or other illicit drugs of abuse to try to reduce mental suffering; therefore the potential for adverse drug interactions to occur is quite high. One drug can affect the absorption, distribution, metabolism, or excretion of a second drug. It was concluded that if physicians are familiar with the various types of pharmacokinetic drug interactions which can occur and their underlying mechanisms, they should be able to provide better patient care and precipitate a lower incidence of iatrogenic adverse drug interactions.

002675 Benyacoub, A.; Roux, J. M. Service Hospitalo-Universitaire de Sante Mentale et de Therapeutique, Centre Hospitalier Sainte-Anne, 1, rue Cabanis, F-75014 Paris, France **/Carpipramine and drug addiction./** Carpipramine et toxicomanies. Encephale (Paris). 4(5, Supplement):595-600, 1978.

In a paper presented at a Conference on the Concept of Inhibition in Psychiatry, held in Monastir, Yugoslavia, October 1978, a study regarding the therapeutic effects of carpipramine in conditions of pharmacodependence to opiates is reported. The withdrawal in 47 subjects by decreased doses of methadone, clinically presenting 42 amotivational syndromes and five depressions is described. Three withdrawal trials using chemotherapy, including carpipramine, failed. It is concluded that carpipramine seems to have an important disinhibitory effect in amotivational syndrome and tolerance is excellent. Lack of desire for this psychotropic drug makes its use safe for drug addicts. 5 references. (Journal abstract modified)

002676 Birkasova, Marie; Birkas, Otto; Flynn, Michael J.; Cort, Joseph H. Psychiatric Treatment Centre, Sternberk, Czechoslovakia **Desmopressin in the management of nocturnal enuresis in children: a double-blind study.** Pediatrics. 62(6):970-974, 1978.

A double-blind study of desmopressin (1-desamino-(8-D-Arg)-vasopressin) in the management of nocturnal enuresis in children is described. Desmopressin or placebo was given by nose drops to 22 children with persistent nocturnal enuresis before going to bed at home. Wetting frequencies per fortnight during desmopressin therapy were significantly lower than either baseline or placebo fortnightly periods. Of the 22 Ss, four failed to react to therapy at all. It is hypothesized that failure to develop a normal diurnal pattern of urine volume and concentration may underly some cases of enuresis. 7 references. (Author abstract modified)

002677 Boland, Frederick J.; Mellor, Clive S.; Revusky, Sam. Memorial University of Newfoundland, St. John's, Newfoundland, Canada **Chemical aversion treatment of alcoholism: lithium as the aversive agent.** Behaviour Research and Therapy (Oxford). 16(6):401-409, 1978.

In an extension of previous animal studies, flavor aversion produced by chemical aversion therapy (CAT) with lithium in the treatment of alcoholism was examined in 25 inpatients showing psychophysiological symptoms of alcohol dependence. An abstinence rate of 36% at 6 month followup for lithium treated patients was significantly better tan the 12% rate found for an equivalent group of patients treated with a disulfuram-like drinking deterrent, calcium carbimide. The rate for the CAT group improved to 47% when eight patients were excluded who did not develop sickness reactions to lithium. Given proper medical precautions, CAT with lithium appears relatively. 36 references. (Author abstract modified)

002678 Bourhis, A.; Boudouresque, G.; Pellet, W.; Fondarai, J.; Ponzio, J.; Spitalier, J. M. Service d'Algologie, Institut J. Paoli-I. Calmettes, 232 bd de St. Marguerite, F-13273 Marseille Cedex 2, France **Pain infirmity and psychotropic drugs in oncology.** Pain (Amsterdam). 5(3):263-274, 1978.

Mechanism of action, indications of psychotropic drugs, and prognosis of cancer pain were investigated in 100 patients. Drugs were selected on the following basis: quiet or depressive patients, trimipramine; agitated patients, levomepromazine; and patients with insomniac pain, trimipramine during day and levomepromazine at night. With regard to the mode of actions of these drugs, it is confirmed that they are not analgesics in the proper sense of the term, for they do not eliminate pain, but their effectiveness to fight against the disability caused by pain is certain. Language invasion and confinement were both reduced. It is cautioned that optimal dose in psychotropic treatment can only be determined by proceeding cautiously, sometimes with putting several drugs to the test, and that the use of narcotics is a main factor of resistance to psychotropic treatment. 8 references.

002679 Calne, Donald B. National Institute of Neurological and Communicative Disorders and Stroke, Bldg. 10, NIH, Bethesda, MD 20014 **Parkinsonism: clinical and neuropharmacologic aspects.** Postgraduate Medicine. 64(2):82-88, 1978.

Clinical and neuropharmacologic aspects of parkinsonism are examined. Topics discussed include: 1) etiology; 2) pathology; 3)physiology; 4) diagnosis; and 5) treatment. Studies have led to a recognition of the importance of certain pathways, such as the nigrostriatal system. This information evolved from the discovery that the neurotransmitter dopamine is depleted in parkinsonism and that restoration of dopamine by the administration of its precursor, levodopa, induces a dramatic therapeutic response in many patients. Still, the tangible benefits have undergone some critical reappraisal with the appearance of late adverse reactions to levodopa. It is suggested that one practical approach to this problem may be to delay starting levodopa therapy and the use of low doses. Use of artificial dopaminergic agonists and selective inhibitors of monoamine oxidose-B has also been investigated. 11 references. (Author abstract modified)

002680 Chien, Ching-piao; Kalayam, Balu; Silver, Reuben. Albany Medical College, Department of Psychiatry, Albany, NY 12208 **The dying and bereaved; the role and status of psychopharmacological agents and analgesics.** Archives of the Foundation of Thanatology. 7(1):9, 1978.

In a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, the status of psychopharmacological agents and analgesics in the management of the dying and the bereaved was examined with a survey conducted with four different professional groups: nursing home physicians, psychiatrists, paramedical mental health workers, and clergymen. A 10 item questionnaire in relation to the general philosophy and attitude toward the usage of psychopharmacological agents and analgesics for specific conditions was answered by 183 people. Intergroup difference on each item revealed differences among the four groups, with clergymen least favorable and nursing home physicians the most favorable in using drug intervention. Findings indicate that clergymen would perfer a natural grief process without drug intervention for the grieving family members, but would not oppose the drug practice for the dying patients. It is concluded that drug treatment for the dying and the bereaved is generally well accepted among professional groups, and careful clinical concern should be directed to the attitude of the consumers.

002681 Christopher, L. J.; Ballinger, B. R.; Shepherd, A. M. M.; Ramsay, A.; Crooks, G. Aberdeen-Dundee Medicines Evaluation and Monitoring Group, Ninewells Hospital, Dundee, Scotland **Drug prescribing patterns in the elderly: a cross-sectional study of in-patients.** Age and Ageing (London). 7(2):74-82, 1978.

A cross-sectional 1 day survey of drug prescribing and drug use in elderly inpatients was carried out in Dundee, Scotland hospitals in 1975. A total of 873 patients were studied, and analyses of prescribing patterns were carried out by patient categories -- medical, surgical, geriatric, psychiatric, and mentally subnormal -- and by major drug groups. While the average number of drugs prescribed per patient on the study day was 3.3, which was not excessive, other results highlighted some possible problems of therapy, including the wide range of drugs used within drug groups, the common use of psychotropic drugs, and dose regimens used in a geriatric population which differed little from general adult dosages and which sometimes involved many administrations per day. Examples are described relating to the use of nitrazepam, phenothiazines, and tricyclic antidepressants. 15 references. (Author abstract modified)

002682 Conners, C. Keith. Department of Psychiatry, University of Pittsburgh, Pittsburgh, PA 15213 **Effect of food additives upon hyperkinetic children. (Unpublished paper).** Final Report, NIMH Grant MH-28458, 1978. 8 p.

Diet responsive hyperkinetic children were maintained on the special elimination diet and were then systematically challenged with food containing artificial colors (food dyes) in a double-blind placebo crossover design to determine if behavior worsens during the active challenge period. Also, the relationship between response to the cytotoxic food allergy test and diet was evaluated, and an attempt was made to determine whether responses to the Feingold Diet are predictable from demographic, social, medical, or other background characteristics. The evidence from three challenge trials was inconsistent with respect to the ability of parents to detect worsening of behavior while their children were receiving the food containing the artificial colors. However, it was found that there appears to be a rather acute, short-term pharmacologic type of effect, which was detectable by laboratory measures but not necessarily to the naked eye, although in one challenge trial parents did notice the effect. Suggestions for further research are given. 21 references.

002683 Conners, C. Keith; Goyette, Charles H.; Newman, Elisa B. Department of Psychiatry, School of Medicine, University of Pittsburgh, Pittsburgh, PA 15213 **Dose-time effect of artificial colors in hyperactive children. (Unpublished paper).** Research Report, NIMH Grant MH-28458, 1978. 14 p.

Sensitive laboratory instruments and observations were used to determine whether hyperactive children who are apparently highly reactive to artificial colors (food dyes) could be demonstrated to show a pharmacological dose time effect. The data show that further experiments to test the hypothesis of a relationship between ingestion of artificial food colors and behavior in children must include a pharmacologic dose response analysis. Inconsistent effects may well represent the borderline effects which would occur with a low dose but pharmacologically active substance. Smaller subjects or those who are especially sensitive would then show an effect, but group studies would probably miss such effects depending upon factors such as age, body mass, time of measurement, and stomach contents. 5 references.

002684 Davis, K. L.; Berger, P. A.; Hollister, L. E.; DoAmaral, J. R.; Barchas, J. D. Veterans Administration Hospital, 3801 Miranda Avenue, Palo Alto, CA 94304 **Cholinergic dysfunction in mania and movement disorders.** In: Jenden, D., Cholinergic mechanisms and psychopharmacology. New York, Plenum, 1978. 885 p. Vol. 24. (p. 755-779).

At the third Symposium on Cholinergic Mechanisms and Psychopharmacology, held in La Jolla, CA, March 1977, a paper discussing trials of choline (Ch) chloride and of Ch chloride compared with physostigmine in patients with tardive dyskinesia, Huntington's disease, and mania was presented. A total of 19 patients received drug injections, and their involuntary movements were videotape recorded. The 100 millimeter visual analog scale, the Patterson Mania Rating Scale, the Brief Psychiatric Rating scale, and weekly structured interviews by a psychiatrist and nurse were used during periods of physostigmine infusion, Ch chloride administration, or placebo dosage. The effects of physostigmine on the involuntary movements of patients with Huntington's disease and tardive dyskinesia, and on the symptoms of mania, support the hypothesis of relative cholinergic underactivity in some patients with these disorders. In agreement with earlier reports, physostigmine did not improve the movements of all the patients with Huntington's disease. Clinical studies with physostigmine suggest the value of developing and testing pharmacological agents that will increase central cholinergic activity. 55 references.

002685 Ellerbroek, Wallace C. Metropolitan State Hospital, Norwalk, CA **Molindone -- a better neuroleptic?** Behavioral Medicine. 5(11):33-37, 1978.

Management of psychiatric patients utilizing molindone, a semisynthetic derivative of rauwolfia, is discussed. Problems with other neuroleptics are noted. Molindone has been found to normalize weight, normalize menstruation in amenorrheic women, is an activating rather than a depressant drug, is an excellent antihallucinogenic, and has no reported human toxicity or persistent extrapyramidal side-effects. While the approved indication for molindone is in the treatment of schizophrenia, good results have been found in the treatment acute and chronic schizophrenia, psychotic depression, acute manic depressive episodes, involutional paraphrenia, and chronic brain syndromes. Copharmacy is discussed, prophylactic use of anti-Parkinsonian drugs is recommended. Justifications for drug use in institutionalized psychiatric populations are also presented. 2 references.

002686 Etienne, P.; Gauthier, S.; Dastoor, D.; Collier, B.; Ratner, J. Douglas Hospital Center, Montreal, Canada **Lecithin in Alzheimer's disease.** Lancet (London). 2(8101):1206, 1978.

The effect on cognitive performance of increasing plasma choline levels through administration of lecithin was studied in seven patients at an early stage of Alzheimer's disease. Subjects were three females and four males of mean age 67 years. Intellectual deterioration had been obvious to their families for less than 3 years. All patients tolerated 25g/day of lecithin without side-effects. With increased dosages side-effects were noted: reduced appetite, abdominal bloating, belching, and diarrhea with fatty stools. The clinical impression was that three patients responded to treatment, seemed to understand instructions more rapidly, became more cooperative, and became less rambling in verbal discourse. New learning ability in these patients improved during treatment, peaked with peak plasma choline levels, and deteriorated after cessation of treatment. No significant improvement in other cognitive tests was noted, and test, though scores achieved when plasma choline values were at a peak tended to be slightly higher than the mean baseline of the group. There were no apparent factors differentiating responders to treatment from nonresponders. The findings suggest that oral doses of lecithen may help some patients with Alzheimer's disease if administered at an early stage of the illness. 9 references.

002687 Ferguson, Tamara; Tourney, Garfield. University of Windsor, Windsor Ont., Canada **Son's reaction to father's death: the need for psychopharmacologic agents?** Archives of the Foundation of Thanatology. 7(1):23, 1978.

In a summary of a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, the behavior patterns of bereaved psychotic adolescent males and their need for psychotherapy instead of treatment based primarily on psychopharmacologic agents were discussed. The problems of the teenage boy who has lost his father are severe, because the event happens at a period in his life when he seeks a male role model to help him solve his growing educational, occupational, financial, and sexual problems and his relationship with is peer group. Some of the excessive reactions may be due to identification with his father and imitation of his patterns of reaction to frustration. It is concluded that the unanticipated consequences of using psychopharmacological agents for this age group appear to be that the adolescent may feel that he is labelled inferior at a period in his life when he has to prove to himself and others that he can perform successfully in different roles.

002688 Fichsel, H.; Knopfle, G. Department of Pediatrics, University of Bonn, Bonn, Germany **Effects of anticonvulsant drugs on thyroid hormones in epileptic children.** Epilepsia. 19(4):323-336, 1978.

The effects of valproate, diphenylhydantoin (DPH), primidone, carbamazepine, or a combination of these drugs on the thyroid hormonal state of 125 epileptic children was investigated. Considerable alterations were found, including decreases in protein bound iron, thyrotoxin (T4), free T4, triiodothyronin (T3), and thyropin hormone (TSH). These changes were dose dependent for valproate, DPH, and carbamazepine. They are based on the displacement of T4 and T3 from their protein binding sites, as well as a more rapid coversion and metabolism of T4 and T3. In the thyroid releasing hormone (TRH) test, marked TSH stimulation resulted in 8% of the 50 patients tested, suggesting a hypothyroid state. The lack of increase in basic TSH in the majority of treated children could result from a hypothalamic drug effect that might result in TRH inhibition. 28 references. (Author abstract modified)

002689 Fredrick, Jerome F. Research Laboratories, Dodge Chemical Company, Bronx, NY **The biochemistry of grief -- is a chemotherapy possible?** Archives of the Foundation of Thanatology. 7(1):15, 1978.

In a summary of a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, the effect of acute grief on the pituitary/adrenal axis with particular attention to the hypersecretion of cortisol and its immunosuppressive reactions was reviewed. The increased susceptibility to infectious disease, bacterial, fungal, and viral, was explored in terms of the altered biochemistry of the bereaved individual. The prophylactic use of antibiotics to bolster failing immunity during the grief period was discussed as well as the use of dexamethasone in preventing hypersecretion in the bereaved. It was concluded that psychological intervention and social supportive measures are of more practical use than chemotherapy because of our lack of knowledge as to the psychophysiological effects of bereavement.

002690 Friedman, Andrzej. Klinika Neurologiczna AM, ul. Lindleya 4, 02-005 Warsaw, Poland **/The use of pizotifen (Sandomigran) for treatment of parkinsonian tremor (preliminary communication)./** Zastosowanie pizotifenu (Sandomigran) w drzeniu parkinsonowskim. Neurologia i Neurochirurgia Polska (Warszawa). 12/28(3):263-267, 1978.

A therapeutic trial undertaken to reduce parkinsonian tremor in 12 patients, via the daily administration of 1.5mg of pizotifen (Sandomigran) is described. A significant reduction of tremor was achieved in two thirds of these patients. No side effects or increased intensity of other Parkinsonian signs were observed. Results are discussed in terms of a possible connection between parkinsonian tremor and a reduced amount of serotonin in the striatum, and in terms of agonistic action of pizotifen in relation to serotonin. 10 references. (Journal abstract modified)

002691 Gadow, Kenneth Dean. University of Illinois at Urbana-Champaign **Psychotropic and antiepileptic drug treatment in programs for the trainable mentally handicapped. (Ph.D. dissertatiou).** Dissertation Abstracts International. 39(5):2866-A, 1978. Ann Arbor, Univ. Microfilms No. 7820938, 283p., 1978.

To determine the prevalence of psychotropic and antiepileptic drug treatment with mentally retarded children and the extent of school participation in the drug regimen, teachers in programs for the trainable mentally retarded (TMR) were surveyed. Teachers reported a total of 3,306 TMR children of which 597 or 18.1% received psychotropic or antiepileptic drugs at some time during the school year. Participation in the antiepileptic and behavior disorder drug regimens was limited. Problems many teachers encountered with drug treatment included: 1) lack of information and training about medication, 2) need for better channels of communication between school, family, and doctor, 3) few guidelines for role of teacher, 4) parent noncompliance with physician instructions, and 5) less than adequate monitoring procedures. (Journal abstract modified)

002692 Gittelman-Klein, Rachel. Queens College, City University of New York, Flushing, NY 11367 **Spectrum of action of psychostimulants and neuroleptics in childhood psychopharmacology.** Advances in Biological Psychiatry (Basel). 2:23-36, 1978.

The use of psychostimulants and neuroleptics in the treatment of childhood behavior disorders is discussed. Psychostimulants can improve performance on a range of cognitive tests and can markedly improve the symptoms of hyperkinesis (overactivity, impulsivity, inattention, and social adjustment). The neuroleptics provide symptomatic relief of hyperactivity, overexcitability, temper outbursts, and unmanageability in a variety of childhood disorders, including psychoses, mental retardation, and hyperkinesis. The neuroleptics are also useful in the treatment of Gilles de la Tourette's syndrome. However, in light of possible neurological side-effects whose ultimate significance is still unknown, the uninterrupted long-term use of neuroleptics is not recommended in children. 42 references. (Author abstract modified)

002693 Green, Brent. School of Social Welfare, 120 Haviland Hall, University of California at Berkeley, Berkeley, CA 94702 **The politics of psychoactive drug use in old age.** Gerontologist. 18(6):525-530, 1978.

Psychotherapeutic drug use among noninstitutionalized older people is explored in relation to the role of the physician, the old patient, and the pharmaceutical industry. A content analysis of recent drug advertisements in leading medical/geriatric journals is described, and the misuse of psychoactive drugs among older people is discussed. Innovative strategies for treatment and prevention are examined. 32 references. (Author abstract modified)

002694 Greenberg, Irwin M. Psychiatric Services, Waterbury Hospital Health Center, Waterbury, CT **General systems approach to the psychopharmacologic treatment of the dying patient.** Archives of the Foundation of Thanatology. 7(1):21, 1978.

In a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, the effects of psychopharmacologic treatment on a dying patient or a bereaved relative and, by means of complex systems interaction, on the patient's interpersonal and sociofamilial world are discussed. The choice of medication, including the use of no medication, whether for the dying person or for the bereaved, depends on a systems analysis of the overall effects on the entire system and its components. For example, even though a patient with terminal illness has reconciled himself to it, to feel the degree of anxiety on the part of a family member may make the situation worse for the patient. It may be desirable to choose an agent which will reduce anxiety in the family member rather than directly treating the patient. It is concluded that the primary goal in using the correct chemical agent is to bring relief to the dying person. The goal of bringing relief iof bringing relief to those about him is secondary.

002695 Hajioff, J. Hill End Hospital, St. Albans, Herts, England **Tardive dyskinesia treatment with DEA.** British Medical Journal (London). 2(6140):834, 1978.

Results of a preliminary study of dihydrogenated ergot alkaloids (DEA) in the treatment of tardive dyskinesia are reported in a letter to the editor. DEA (4 to 5 mg daily) was administered to six long-term phenothiazine patients over a 6 week period. It was found that all responded within 2 to 4 weeks, and by 6 weeks one had lost all symptoms of tardive dyskinesia and the others had only mild symptoms. A more extended study is planned. It is suggested that DEA may work by correcting disturbed striatal dopamine activity or by improving metabolism of cells in the area by increased oxygenation. 1 reference.

002696 Halliday, Roy; Gnauck, Katie; Rosenthal, Joseph R.; McKibben, Jane L.; Callaway, Enoch. Langley Porter Institute, University of California, San Francisco, CA 94143 **The effects of methylphenidate dosage on school and home behavior of the hyperactive child. (Unpublished paper).** Research Report, NIMH Grant MH-22149, 1978, 24 p.

The clinical response of hyperactive children treated with methylphenidate was investigated via teacher and parent ratings. Methylphenidate was administered to 15 hyperactive boys using four dosages (.00, .16, .33, and .66mg/kg) and a within subjects

design. Increasing dosage improved teacher ratings on the Conners Teacher Rating Scale (ATS) as well as estimates of academic output and the quality of the child's week. Dosage also affected parents' ratings. Parents' estimates of the quality of the child's week improved up to the .66mg/kg dosage. Scores on the Werry-Weiss-Peters activity scale improved up to the .33mg/kg. Drug response on the Conners ATS depended on age, with older children showing better responses to the medication. The academic output variable showed no age relationship. The relationship between these findings and previous research are discussed, along with treatment implications. 9 references. (Author abstract modified)

002697 Hartford, J. T.; Smith, R. C.; Leevathi, D. E.; Smith, C. H.; Hu, R.; Varner, R.; Schoolar, J. C. Texas Research Institute of Mental Sciences, Houston, TX 77030 **Neuropharmacological changes of aging.** Gerontological Society: 31st Annual Scientific Meeting. 18(5, Part 2):80, 1978.

A summary of a paper read at the 31st Annual Meeting of the Gerontological Society, held in Dallas, November 1978, is presented. Neuropharmacological changes of aging were studied via research on blood levels and pharmacokinetics of two psychiatric drugs, nortriptyline and butaperazine, in elderly psychiatric patients. Steady-state blood levels were analyzed when the patients were on regular treatment with the medication, as well as pharmacokinetics after a single dose of the medication. It was concluded that since blood levels of the two drugs have been shown to be related to therapeutic side-effects, the blood levels in older patients should have direct clinical relevance. (Author abstract modified)

002698 Horn, Alan S. Department of Pharmacy, University of Groningen, Groningen, The Netherlands **Effect of psychotropic drugs on brain biogenic amine systems.** Advances in Biological Psychiatry (Basel). 2:87-95, 1978.

The neurochemical mechanisms of action of the main groups of psychotropic drugs used in child psychiatry (psychostimulants, neuroleptics, tricyclic antidepressants, and benzodiazepines) are outlined. Amphetamine and methylphenidate, the two stimulants most commonly used in treating hyperkinetic children, appear to act by different mechanisms; amphetamine may interact with a newly synthesized catecholamines, releasing dopamine and inhibiting noradrenaline uptake, whereas methylphenidate may act predominantly on stored catecholamines, inhibiting their uptake. The tricyclic antidepressants act by inhibiting the uptake of noradrenaline and 5-hydroxytryptamine. The neuroleptics, which are used in the treatment of the major psychoses such as schizophrenia, bring about their antipsychotic effects by blocking dopamine receptors in the brain. The mechanism of action of the benezodiazepines is not well understood; the drugs mimic gamma-aminobutyric acid, and reduced 5-hydroxytryptamine turnover. Specific benzodiazepine receptors have also been identified in the brain. 57 references. (Author abstract modified)

002699 Hosokawa, Kiyoshi; Kugoh, Toshiaki. Dept. of Neuropsychiatry, Okayama University Medical School, Okayama, Japan **Prognosis in patients with epilepsy -- special reference to change in types of seizure and ingestion of prescribed drugs --.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 32(3):447-448, 1978.

The prognosis for patients with epilepsy is discussed in relation to change in types of seizure and ingestion of prescribed drugs. The 120 adult Ss who had been under observation for a mean duration of 11.5years were divided inot three groups: transition of independent grand mal seizure, transiton of independent psychomotor seizure, and transition of grand mal and psychomotor seizure combination.

002700 Hoyumpa, Anastacio M., Jr. Division of Gastroenterology, Veterans Administration Hospital, Nashville, TN 37203 **Disposition and elimination of minor tranquilizers in the aged and in patients with liver disease.** Southern Medical Journal. 71(2):23-28, 1978.

In a paper presented at the McLean Hospital Symposium held in Dallas, November 1977, the effect of age and liver disease on the disposition and elimination of minor tranquilizers is discussed. It is suggested that because of altered drug disposition, the response of the elderly patient may be more profound than that of the young adult and may be manifested by exaggerated sedation. This altered response or increased cerebral sensitivity is similar in patients with hepatic dysfunction. It is concluded that based on pharmacokinetic data, oxazepam and lorazepam would seem to be more suitable than diazepam and chlordiazepoxide for use in the elderly and in patients with liver disease. 22 references.

002701 Itil, Turan M.; Reisberg, B. Division of Biological Psychiatry, New York Medical College, Tarrytown, NY **Pharmacologic treatment of aggressive syndromes.** Current Psychiatric Therapies. 18:137-142, 1978.

The pharmacologic treatment of aggressive syndromes is discussed. It is asserted that proper treatment requires a knowledge of etiologic determinants, each of which requires different interventions. The treatment of extreme emergency aggression, acute emergency, persistent acute aggression, episodic aggression, and aggression in children is detailed. The potential future value of marihuana, endorphins, and enkephalins in the treatment of aggression is cited. 30 references.

002702 Kast, Eric C. no address **On being old and on dying.** Archives of the Foundation of Thanatology. 7(1):16, 1978.

In a summary of a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, characteristics of the psychologic aging process and the impact of terminal diseases on the aging individual were discussed. Isolation and depression are the main characteristics of the aging process. Hypochondriasis may be a defense against isolation. In the terminally ill patient, anticipation becomes less and less useful and more and more painful. LSD, which attenuates anticipation for as long as 2 weeks after administration, can give the patient's immediate sensory input an overwhelming role in his life while relieving him of the burden of inappropriate anticipation. (Author abstract modified)

002703 Kendler, Kenneth S.; Weitzman, Richard E.; Rubin, Robert T. Rubin: Dept. of Psychiatry, Harbor General Hospital, Torrance, CA 90509 **Lack of arginine vasopressin response to central dopamine blockade in normal adults.** Journal of Clinical Endocrinology & Metabolism. 47(1):204-207, 1978.

The effect of central neurotransmitter dopamine (DA) in the control of arginine vasopressin (AVP) release in man was investigated in a controlled clinical setting. Haloperidol, a central nervous system dopamine blocker, was given intramuscularly to seven normal volunteers at a dose level known to have central nervous system effects. Plasma prolactin levels rose sharply in response to haloperidol, but plasma arginine vasopressin levels did not change significantly. These data do not support the hypothesis of a prominent dopamine neurotransmitter regulation of arginine vasopressin secretion. 25 references. (Author abstract modified)

002704 Klein, Donald F., Gittelman-Klein, Rachel. New York State Psychiatric Institute, 722 West 168th Street, New York, NY 10032 **Drug treatment of separation anxious and depressive illness in children.** Advances in Biological Psychiatry (Basel). 2:50-60, 1978.

The pharmacological treatment of depression and separation anxiety in children is discussed. Although the two illnesses are clearly linked, they do not appear to be identical in children. Treatment with imipramine has been shown to be beneficial in children with depressive illness and secondary separation anxiety. Other studies of the beneficial effects of antidepressants in childhood depression have also been reported, but these studies have generally not been properly controlled. 32 references. (Author abstract modified)

002705 Klicpera, Chr. Kraepelinstr. 10, D-8000 Munchen 40, Germany **/Treatment of children with stimulant drugs./** Die Stimulantienbehandlung bei Kindern. Zeitschrift fur Kinder- und Jugendpsychiatrie (Stuttgart). 6(2):177-196, 1978.

Diagnostic and prognostic indications for the treatment of children with stimulants are discussed. The principal indications for prescription of amphetamines or related stimulants are hyperkinetic syndromes and minimal cerebral dysfunction. Improvement can be expected in about 50% of cases. Children with motor restlessness tend to show the most favorable results, especially if inattentiveness is present. The efficacy of stimulant drugs can be judged from the reports of several independent observers. At best, drugs can complement other therapeutic methods, which are to be tailored to the child's specific difficulties. 92 references.

002706 Krogh, H. J.; Khan, M. A.; Fosvig, L.; Jensen, K.; Kellerup, P. State Hearing Centres, Research Laboratory for Technical Audiology, University Hospital, Odense, Denmark **N1-P2 component of the auditory evoked potential during alcohol intoxication and interaction of pyrithioxine in healthy adults.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 44(1):1-7, 1978.

The auditory evoked potential was used to assess the effect of alcohol intoxication (1g/kg) and pyrithioxine (7mg/kg) on nine adult subjects. It s components in the latency range 50-250 msec (N1-P2) were studied for 6g 30 min, during a constant level of alertness. Four periods were considered: alcohol alone, alcohol plus pyrithioxine, pyrithioxine plus alcohol, and placebo. With alcohol alone the N1-P2 amplitude was small in the first part of the test and large in the second part as compared to placebo values. Pyrithioxine antagonism was greatest after alcohol had been resorbed. The placebo period indicates that amplitude changes were not due to long-term habituation, when the subject was kept alert. 8 references. (Author abstract)

002707 Kutscher, Austin H.; Kutscher, Lillian. Foundation of Thanatology, 630 W. 168 Street, New York, NY 10032 **Use of psychopharmacologic and analgesic agents in the clinical and psychosocial care of the dying patient and the bereaved.** Archives of the Foundation of Thanatology. 7(1):1, 1978.

In a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, the proceedings of an earlier symposium in 1971 were summarized and the focus of the present symposium detailed. In 1971, a group of multidisciplinary investigators and practitioners convened to explore the beneficial use of such agents and to determine the hazards that might be involved in their use. Investigations involving the potential of LSD therapy for terminal patients in a controlled environment were reported. The conference was informed of the effective use of diamorphine for the control of pain in the terminal cancer patient. After the proceedings of this symposium were published, professionals in many disciplines became more and more impressed by the need to reevaluate, according to their own perspectives, contemporary institutions and systems for the care of the terminally ill patient and the members of his family. The present symposium emphasizes advances in the use of psychopharmacology and analgesia for dying patients, the role of psychopharmacology in the care of survivors, and changing perceptions of this type of treatment.

002708 Lake, C. Raymond; Ziegler, Michael; Coleman, Michael; Kopin, Irwin J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Effect of clonidine on sympathetic nervous system (SNS) function in hypertensive patients. (Unpublished paper)** Bethesda, MD, NIMH, 1978. 1 p.

The effect of clonidine on sympathetic nervous system (SNS) functioning in seven hypertensive patients, aged about 34.3years was investigated. Ss were treated with 0.2mg/day, and alterations in blood pressure, heartrate (HR), and plasma levels of norepinephrine (NE) were examined in supine and standing positions after 1 and 5 weeks of treatment. Blood pressure and supine HR were diminished by clonidine. After 1 week, plasma NE was reduced by 248 plus or minus 46 pg/ml (supine) and 361 plus or minus 125 pg/ml (standing) without further significant decrease after continued treatment. The proportional increments in plasma NE induced by standing up were similar before and after treatment, although absolute levels were lower after the drug. Results are consistent with a readjustment of gain in the baroreceptor reflex as the mechanism for lowering blood pressure by clonidine. (Author abstract modified)

002709 Leibowitz, Morton; Sunshine, Abraham. 907 Fifth Avenue, New York, NY 10021 **Long-term hypnotic efficacy and safety of triazolam and flurazepam.** Journal of Clinical Pharmacology. 18(5-6):302-309, 1978.

The hypnotic effectiveness of 0.6mg triazolam compared to that of 30mg flurazepam when administered to insomniacs was compared. At the dosages tested, triazolam had a significantly faster onset of activity than flurazepam. No tolerance development occurred for the two drugs. Side-effects occurred more often on flurazepam than on triazolam, and the number of patients experiencing side-effects was significantly higher in the flurazepam group. Additionally, the number of patients reporting drowsiness or grogginess was also higher in the flurazepam group. 5 references. (Author abstract modified)

002710 Ling, Walter. Drug Dependence Treatment Center, Veterans Administration Hospital, Sepulveda, CA 91343 **Levo-alpha-acetylmethadol (LAAM) for opiate addiction.** Current Psychiatric Therapies. 18:173-180, 1978.

The use of levo alpha-acetylmethadol (LAAM) as an alternative to methadone in the treatment of opiate addiction is discussed. LAAM is a methadone derivative currently being tested for its applicability to the maintenance treatment of narcotic addiction. The clinical literature and current status of LAAM research is reviewed. In a current study involving 2,500 patients, results indicate favorable retention and safety. It is argued that LAAM may be preferable to methadone because of its less frequent ingestion schedule eliminating the need for take home medication. The danger of acute overdose, which is increased by the delayed onset of action, is noted. 20 references.

002711 Lingjaerde, O.; Berglund, J.; Bratland, S. Z.; Christensen, J. E.; Eikrem, A.; Hercz, I.; Joakimsen, R.; Moe, F.; Olsen, T. I.; Stenvold, S. E. University of Troms, 9010 Asgard, Norway **Alimemazine (trimeprazine, Vallergan) as a hypnotic in**

general practice patients: a controlled comparison with nitrazepam. Current Therapeutic Research. 24(4):388-396, 1978.

A group comparison of alimemazine (trimeprazine, 20mg) and nitrazepam (5mg) were made in a double-blind study of 61 ambulatory insomniacs. An initial treatment period of 1 week was followed by another 2 or 3 weeks on the same drug for those who wanted to continue. Various aspects of sleep were assessed subjectively. Significantly more patients on nitrazepam (29 of 33) than on alimemazine (15 of 26) continued for another 2 weeks. After 1 week, sleep was significantly better in the nitrazepam group, especially in sleep latency and total assessment of sleep. Nitrazepam seemed to have a particularly favorable effect in elderly patients. In the alimemazine group, favorable effect was seen especially in patients with late insomnia. After 3 weeks, several sleep variables showed a nonsignificant trend towards better effect of alimemazine than of nitrazepam, and there was a further significant improvement in the alimemazine group, but not in the nitrazepam group. The frequency of side-effects was moderate, and not significantly different in the two drug groups. 6 references. (Author abstract modified)

002712 Lipani, John A. no address **Preference study of the hypnotic efficacy of triazolam 0.125 mg compared to placebo in geriatric patients with insomnia.** Current Therapeutic Research. 24(4):397-402, 1978.

A 2 night double-blind crossover trial comparing the hypnotic effectiveness of triazolam 0.125mg to placebo was conducted in 42 geriatric patients suffering from insomnia. One patient discontinued after night 1 because of side-effects. Results indicate that triazolam was significantly better than placebo in helping the patients sleep, reducing time of sleep onset and increasing duration of sleep. Triazolam tended to be better than placebo, but not significantly on the number of nocturnal awakings and feeling of alertness in the morning. After the second night of treatment, patients were asked which night, if either, they slept best. Analysis of the responses showed triazolam was significantly better than placebo. Twenty-seven of the 41 patients preferred triazolam, 9 preferred placebo, and 5 had no preference. More side-effects were reported on triazolam than placebo but they were those that are usually associated with this class of benzodiazepines. 9 references. (Author abstract modified)

002713 Marx, Jean L. no address **Parkinson's disease: search for better therapies.** Science. 203(4382):737-738, 1979.

Current research into new therapies for Parkinson's disease, a degenerative brain disorder, is discussed. The use of L-dopa has been found to cause disabling side-effects after about 3 years of treatment. The action of the neurotransmitter dopamine, which is deficient in the brains of parkinsonian patients, is being investigated. It has been discovered that there are at least two kinds of dopamine receptors, and it is reported that insufficient dopamine at one of the receptors may contribute to the development of the neurological features of Parkinson's disease. Because dopamine cannot pass the blood-brain barrier, agents that mimic the action of dopamine are being clinically tested. Several of these agents are described.

002714 McKnew, Donald H., Jr. Biological Psychiatry Branch, National Institute of Mental Health, Bldg 10, 3N-204, Bethesda, MD 20014 **Use of psychotropic medication in adolescent psychiatry. (Unpublished paper).** Bethesda, MD, NIMH, 1978. 15 p.

A review of psychopharmacology as it applies to adolescents is presented. Drugs that are helpful in the treatment of anorexia nervosa are mentioned, including the chlorpromazine group, amitriptyline, and cyproheptadine. Depression proper is very responsive to either the tricyclics, monoamine oxidase inhibitors, or lithium. The treatment dosages and consequent side-effects of these drugs are described. The administration of minor and major tranquilizers is discussed. Minor tranquilzers are not very useful for adolescents because of problems of addiction. Major tranqulizers are used in adolescents exactly as they are with adults, for schizophrenia and other psychotic states. It is concluded that the psychopharmacology of adolescents is very similar to that of adults. It is primarily in management areas that differences arise. 24 references.

002715 Mitarski, Jan; Polewka, Andrzej; Treter, Aleksander; Zieba, Andrzej. Klinika Psychiatryczna AM, ul Kopernika 21 31-501 Kracow, Poland **/Electroconvulsive therapy with diazepam administration (preliminary report)./** Wstrzasy elektryczne z zastosowaniem diazepamu (doniesienie wstepne). Psychiatria Polska (Warszawa). 12(5-6):587-590, 1978.

A preliminary report on electroconvulsive therapy preceded by an intravenous diazepam injection is presented. The study was conducted using 100 patients, ranging in age from 17 to 54 years, 66 male and 34 female, who were diagnosed as depressive phobic or depressive delusional. Nine hundred electroconvulsant treatments, usually 8 to 10 per patient were conducted. Two to five minutes prior to treatment the patients were given diazepam. The control group of 100 patients were given electroconvulsant therapy by the traditional method. It was found that intravenous injection of diazepam (relanium) before treatment gives a five fold decrease in surgical complications, makes the patients less fearful of the treatment and prevents psychomotor agitation which is likely to occur after electroconvulsant treatments carried out by the traditional method. The efficacy of electroconvulsant therapy combined with diazepam injection was compared with that obtained without use of the drug. The treatment effects were found similar, but superior in quality, to those obtained with ECT combined with the use of succinylochine. 7 references. (Journal abstract modified)

002716 Morselli, Paolo L.; Cuche, Henry; Zarifian, Edouard. Department of Clinical Research, Synthelabo, LERS, 58, rue de la Glaciere, F-75621 Paris Cedex 13, France **Pharmacokinetics of psychotropic drugs in the pediatric patient.** Advances in Biological Psychiatry (Basel). 2:70-86, 1978.

Pharmacokinetic data for major and minor tranquilizers, hypnotic drugs, and stimulants in children is reviewed. The lack of scientific information in this area increases the risk of adverse toxic reactions and impairs therapeutic efficacy. The data that is available shows important differences in the disposition of drugs during development. Newborns, infants, children, and adults differ from both pharmacokinetic and therapeutic points of view. It is concluded that routine monitoring of drug plasma levels in children is the only way to obtain information on the therapeutic and toxic thresholds for psychotropic drugs in pediatric patients. 94 references. (Author abstract modified)

002717 Moss, Steven A. Jewish Chaplaincy Service, Memorial Sloan-Kettering Cancer Center, New York, NY **The "getting of one's house in order' and pharmacologic agents.** Archives of the Foundation of Thanatology. 7(1):12, 1978.

In a summary of a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, areas of conflict in the usage of pharmacologic agents for the terminally ill patient who is in pain or discomfort were discussed. Questions were raised about the effect of a growing leniency toward the usage of potent pharmacologic agents on the patient's need to communicate spiritual and emotional concerns at this critical time. Such a usage of potent drugs might be at odds with the ideal of ""getting one's house in order" or even

the process and ritual of confession. It is suggested that these possible areas of conflict in terms of the usage of these pharmacologic agents might be solved for the ultimate good of the terminal patient.

002718 Muller, H. F.; Dastoor, D. P.; Klingner, A.; Cole, M.; Boillat, J. Douglas Hospital Centre, 6875 LaSalle Boulevard, Verdun, Quebec, Canada H4H 1R3 **Amantadine in senile dementia: electroencephalographic and clinical effects.** Journal of the American Geriatrics Society. 27(1):9-16, 1979.

Nineteen patients with senile brain disease including two with parkinsonian symptoms were treated with amantadine in an oral dosage of 200-300mg daily. Seven showed definite clinical benefits such as increased alertness and decreased agitation, and two others showed slight benefits. However, in only one instance was the benefit maintained without complications. Toxic effects such as overactivity, anxiety, and visual hallucinations were observed in eight patients. Withdrawal effects (e.g.,lethargy and staggering) occurred when amantadine was discontinued. The EEGs of all 19 patients showed a frequency increase, chiefly of occipital alpha activity, and sometimes a return to normal, irrespective of clinical changes. Toxic side effects were associated with particularly prominent EEG acceleration. In 10 of the 19 patients, the clinical changes were further validated by additional psychologic assessments. It is concluded that although the value of amantadine is limited when given in this way to patients with senile brain disease, it is important to observe its effects in drug combinations aimed at correction of neurotransmitter imbalances. 22 references. (Author abstract)

002719 Nanba, Shinpei. Iwakuni National Hospital, Yamaguchi, Japan **Effect of pyridoxine (V-B6) on L-dopa therapy of parkinsonism -- in combined therapy of L-dopa with peripheral decarboxylase inhibitor.** Iryo (Therapeutics) (Tokyo). 32(7):866-873, 1978.

The effect of pyridoxine in the combined treatment of L-dopa plus peripheral decarboxylase inhibitor to treat parkinsonism was clinically and experimentally examined. Effect of pyridoxine was detected in 6 of 12 parkinsonian patients who had been treated with L-dopa/MK486. Improvement of bradykinesia was observed in four of the six cases. Remarkable dyskinesia was induced in one case, and an effect on tremor was observed in another one. Experimental results using monkeys and rats are reported. It is concluded that the administration of pyridoxine should be tried in cases where administration of L-dopa with peripheral decarboxylase inhibitor shows unsatisfactory results in the treatment of parkinsonism. 17 references. (Journal abstract modified)

002720 no author. no address **Ergot drugs help severe Parkinson's.** Medical World News. 19(22):30, 1978.

Two studies of the use of ergot drugs in the treatment of severe Parkinson's disease are reported which indicate that bromocriptine and lergotrile, given singly or with L-dopa, can decrease neurological symptoms in patients with advanced Parkinson's disease. Because the two compounds have mixed agonist/antagonist properties at both presynaptic and postsynaptic dopamine receptors, the therapeutic effects of these agents support the hypothesis that several receptor groups are affected in Parkinson's disease. Improvement in mental status was the same with both drugs, but involuntary movements were more pronounced with bromocriptine, whereas liver toxicity was more severe with lergotrile.

002721 Nunn, R. Gregory. Chicago Habits Clinic, 626 Grove Street, Suite 201, Evanston, IL 60201 **Maladaptive habits and tics.** Psychiatric Clinics of North America. 1(2):349-361, 1978.

An overview of current theories and diagnostic criteria regarding maladaptive habits and tics, as well as standard treatment procedures and their results, is presented. The habit reversal and regulated breathing techniques are covered, along with suggestions for monitoring progress. It is reported that psychotherapy is about 25% effective, negative practice about 30%, and operant procedures about 75% effective. Haloperidol is about 50% effective for persons with Gilles de la Tourette syndrome, while the other 50% suffer severe drug side-effects. Habit reversal and regulated breathing were found to be about 95% at 1 week, and 99% at the end of 1 month. It is suggested that, while habit reversal and regulated breathing approaches have not yet been applied with a large number of persons with very severe Gilles de la Tourette syndrome, they do appear to be more effective than alternative methods in the treatment of maladaptive habits, tics, and stuttering. 42 references. (Author abstract modified)

002722 Parnes, Yvonne M. Community Health Program, Queens-Nassau, Inc., New Hyde Park, NY **Merciful methadone.** Archives of the Foundation of Thanatology. 7(1):8, 1978.

In a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, the benefits of using methadone for pain relief for the terminally ill patients and to enable home care by the involved families are described. A case history is presented of a female patient with metastatic disease who, after months of pain, responded after 2 days of methadone by being able to sleep nights and to communicate with clarity. The family was able to care for her, to show signs of anticipatory grief and support, to avoid the sense of being medically abandoned, to avoid the tensions created by the confrontation with intractable pain, and to return to some semblance of daily living. It is concluded that methadone can become a new ally in helping the patient, the family, and the professional accept the many facets of terminality.

002723 Perry, Thomas L.; Wright, James M.; Hansen, Shirley; MacLeod, Patrick M. Dept. of Pharmacology, University of British Columbia, Vancouver, British Columbia, Canada V6T 1W5 **Isoniazid therapy of Huntington disease.** Neurology. 29(3):370-375, 1979.

Clinical and biochemical changes in seven patients with Huntington disease given isoniazid (INH) in dosages three to five times greater than normally used in tuberculosis are described. Of six patients treated long enough to be clinically evaluated, one showed marked and two other showed significant improvement. High dose INH therapy carries serious toxic risks, which are influenced by patients' acetylator phenotypes. Nevertheless, results are sufficiently promising to warrant further controlled trials of INH or other gamma-aminobutyric acid transferase inhibitors in Huntington disease. 34 references. (Author abstract modified)

002724 Rapoport, Judith L. no address **Antidepressant drug use in child psychiatry. (Unpublished paper)** Bethesda, MD, NIMH, 1978. 33 p.

Current concepts of depression in childhood are reviewed and evidence for the validity of the diagnosis, the use of antidepressants in child psychiatry, and methodological issues in research with children are discussed. The evidence suggests that, although childhood depressive disorder can occur, it is rare, and caution should be exercised in employing this diagnosis. Pharmacological investigations with antidepressants have provided a variety of clinically useful drugs, but the efficacy of these agents in pediatric conditions appears to be independent of antidepres-

sant effect. Children respond to many of these agents differently than do adults. It is suggested that before puberty, some difference in physiological status, such as immaturity of the neurotransmitter systems, or a difference in receptor sensitivity, provides protection against drastic and sustained mood alteration, unless extremely dire conditions are present. Intensive studies of high-risk children as they reach puberty might illuminate the relative immunity of children to psychological depression. 79 references.

002725 Regelson, William; West, Brian. Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Use of psychopharmacologic and analgesic agents in the clinical and psychosocial care of the dying patient and the bereaved.** Archives of the Foundation of Thanatology. 7(1):6, 1978.

In a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, the physician's responsibility in choosing and using psychopharmacologic and analgesic agents in the clinical care of the dying patient and the bereaved is discussed. The side-effects of drugs, including sleep, depersonalization, and a cumulative Parkinson-like toxicity, are often dose related and disturbing to the patient and family. Placebo responses are valid, and the positive conditioning role of the physician and nurse must be backed by a strong belief system in the value of their physical presence and the effectiveness of their drugs. It remains the individual responsibility of the physician to ensure the patient's comfort. The best medication for the grieving family is the knowledge that all has been done that could be done. It is concluded that psychopharmacologic agents to support patients and families during the critical period of dying must not be used as a substitute for human concerns which allow for the expression of feeling or the exchange of values.

002726 Rinne, U. K.; Koskinen, V.; Laaksonen, H.; Tenovuo, O. Department of Neurology, University of Turku, SF-20520 Turku 52, Finland **Angiotensin converting enzyme in the parkinsonian brain.** Annals of Neurology. 4(5):483, 1978.

Alterations of angiotensin converting enzyme (ACE) during Parkinson's disease were studied. Postomortem brain samples from two women and two men with Parkinson's disease were dissected for biochemical analysis and compared with corresponding control brain samples from six patients without extrapyramidal disorders. The activity of ACE in all brain regions studied did not differ in patients with Parkinson's disease and controls. Moreover, treatment with levodopa and benserazide had no evident effect in the parkinsonian brain. The findings support the effect of selective depletion of ACE activity in the corpse striatum in Huntington's chorea and provide further evidence of the occurrence of different biochemical and pathological changes in the extrapyramidal system of choreic and parkinsonian patients. 5 references.

002727 Robertson, Clive C.; Sellers, Edward M. Sellers: 33 Russell St., Toronto, Ontario, M5S 2S1, Canada **Alcohol intoxication and the alcohol withdrawal syndrome.** Postgraduate Medicine. 64(6):133-138, 1978.

Alcohol intoxication and the consequences of the abrupt cessation of alcohol intake, both of which may produce significant morbidity and even mortality, are described. Hepatic metabolism of ethanol is usually rapid, and in most cases general supportive care of the intoxicated patient is all that is required. Abrupt cessation of intake gives rise to the alcohol withdrawal syndrome. The fundamentals of treatment are careful assessment of the patient and judicious use of a benzodiazepine. Severe reactions require hospitalization and oral or intravenous administration of a benzodiazepine. Other pharmacotherapy may include phenytoin for withdrawal seizures, haloperidol for severe agitation or hallucinations, or propranolol. 16 references.

002728 Sakamoto, Yoshimasa; Kasahara, Masaru; Satouchi, Hiroshi; Amago, Akihisa; Sageshima, Masato. Dept. of Pediatrics, Kansai Medical School, Moriguchi, Japan **Long-term prognosis on recurrence of seizures among children with epilepsy after drug withdrawal-elimination.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 32(3):435-437, 1978.

Long-term prognosis on recurrence of seizures among children with epilepsy after drug withdrawal/elimination is described. Twelve cases out of 110 children experienced recurrences, which occurred between 3 months to 3 years after drug elimination, but there were no recurrences later than 3 years to 10 years after drug elimination. No asymmetry or seizure discharge was found in EEG later than 3 years after drug elimination. 5 references.

002729 Salem, S. A. M.; Rajjayabun, P.; Shepherd, A. M. M.; Stevenson, I. H. Department of Therapeutics and Pharmacology, Queen's University, Belfast, Ireland **Reduced induction of drug metabolism in the elderly.** Age and Ageing (London). 7(2):68-73, 1978.

Young and elderly subjects were given the hypnotic dichloralphenazone (Welldorm) in a dose of 20mg/kg nightly for 2 weeks and the extent of liver microsomal drug metabolism was assessed from alteration in the plasma elimination of quinine and antipyrine (phenazone). With both indices, there was a significant increase in plasma drug clearance in young subjects following dichloralphenazone treatment but no significant alterations occurred in the elderly group. The results indicate that, in addition to being less able to metabolize some drugs, elderly patients show a reduced induction response. They may therefore be less likely to become tolerant to those drugs which are inactivated by metabolism. 15 references. (Author abstract)

002730 Sanders-Woudstra, J. A. R. Department of Child Psychiatry, Sophia Children's Hospital, Rotterdam, The Netherlands **The importance of psychodynamics in relation to psychopharmacology.** Advances in Biological Psychiatry (Basel). 2:61-69, 1978.

The role of drug treatment in childhood psychiatric disorders is considered. The importance of a combined approach in the analysis and treatment of these disorders is stressed. The proper setting for drug treatment and the necessary supporting measures are discussed. 11 references. (Author abstract modified)

002731 Scranton, Thomas R.; Hajicek, Joseph O.; Wolcott, George J. Hajicek: 2345 S. Rogers, Springfield, MO 65804 **The physician and teacher as team: assessing the effects of medication.** Journal of Learning Disabilities. 11(4):205-209, 1978.

The classroom teacher was used as an information source to the physician to determine the effects of medication on the classroom learning of children described as learning disabled. The teacher administered five educationally relevant tasks daily to two boys receiving continuous Ritalin dosages interspersed with Ritalin or placebo dosages on a random basis. The tasks were brief, producing objective, descriptive data for interpretation by the physician/teacher team and assessing skills directly related to classroom learning activities. Results indicate that teacher collected data were highly reliable; three of the five dependent variable measures were sensitive to the effects of Ritalin, and the cooperation of physician and teacher supplies the physician with needed information in choosing the medication

and the appropriate dosage for the child in the learning environment. 10 references. (Author abstract)

002732 Sellers, Edward M. Division of Clinical Pharmacology, Addiction Research Foundation, University of Toronto, Toronto, Ontario, Canada **Antianxiety drugs in alcohol withdrawal.** Current Psychiatric Therapies. 18:157-163, 1978.

The pharmacologic management of the alcohol withdrawal reaction is discussed. Drug treatment of alcohol withdrawal relieves anxiety, a frequent complaint in withdrawal. The use of ethyl alcohol, haloperidol, lithium, propranolol, and benzodiazepines is outlined. Guidelines for a full assessment of the patient regarding agitation, anxiety, tremor, extreme agitation, seizures, and hallucinations are presented. It is concluded that antianxiety agents are effective against most aspects of withdrawal except seizures and hallucinations, and that the benzodiazepines are the best available. 33 references.

002733 Seyler, Lloyd Everett, Jr.; Canalis, Ernesto; Spare, Steven; Reichlin, Seymour. Building 5, Veterans Administration Hospital, Newington, CT 06111 **Abnormal gonadotropin secretory responses to LRH in transsexual women after diethylstilbestrol priming.** Journal of Clinical Endocrinology & Metabolism. 47(1):176-183, 1978.

Pituitary luteinizing hormone (LH) and follicle stimulating hormone (FSH) secretory responses to synthetic luteinizing hormone releasing factor (LRH) were measured in nine female transsexuals with normal menstrual cycles before and after a 7 day course of treatment with diethylstilbestrol (DES) to determine whether female transsexuals have abnormal hypothalamic-pituitary feedback control. Control groups included five heterosexual women and seven heterosexual men. Pituitary responses to LRH in heterosexual women studied in the early follicular phase increased markedly after DES administration and were clearly different from responses in men, which were all inhibited by DES. Responses to LRH in nine transsexual women studied in the early follicular phase differed strikingly from normal women in that gonadotropin responses were not enhanced by DES. The finding that the responses of female transsexuals to DES and LRH were intermediate between the female and the male patterns suggests that a biological abnormality accompanies the psychological abnormality in such patients. 52 references. (Author abstract)

002734 Shomrat, N.; Vardi, J.; Streifler, M.; Rabey, J.; Flechter, S.; Rinott, J. Department of Neurology, Tel-Aviv Municipal and Governmental Medical Center, Ichilou Hospital, Tel Aviv, Israel **The therapeutic efficacy of Sinemet in parkinsonian patients on prolonged anticholinergic therapy.** Current Therapeutic Research. 24(4):403-414, 1978.

The effect of the administration of an L-dopadecarboxylase inhibitor combination (Sinemet) was assessed in parkinsonian patients on prolonged anticholinergic therapy. In an open, controlled study, 25 patients (average age 65 years, average disease duration 3.66 years) were clinically repeatedly evaluated during a 10 week trial period. Clinical signs were graded according to a modification of the Northwestern University rating scale for Parkinson's disease. The addition of Sinemet resulted in a rapid, marked, consistent objective and subjective improvement. The global impairment score was significantly reduced by 65.8%. This improvement was found to be more conspicuous in the group of younger patients and in those with a shorter duration of the disease. Rarely encountered side-effects of Sinemet addition were mild and disappeared spontaneously or after adjustment of dose or mode of administration of the drug. 6 references. (Author abstract)

002735 Smith, C. M.; Swash, M.; Exton-Smith, A. N.; Phillips, M. J.; Overstall, P. W.; Piper, M. E.; Bailey, M. R. Dept. of Pharmacology and Therapeutics, London Hospital Medical College, London E1 2AD, England **Choline therapy in Alzheimer's disease.** Lancet (London). 2(8084):318, 1978.

A double-blind, placebo controlled study of the effects of choline on memory in patients with Alzheimer's diesease was undertaken to investigate the hypothesis that impairment of presynaptic cholinergic neurotransmission may cause the characteristic short-term memory disorder found in the early stages of Alzheimer's disease. No significant differences between drug and placebo emerged on any of the tests. Nevertheless, three patients seemed less confused after 2 weeks of choline treatement. There was an exacerbation of preexisting urinary incontinence in three patients due to detrusor instability, and gastrointestinal discomfort occurred in some patients. 11 references.

002736 Snider, William D.; DeMaria, Alfred A., Jr.; Mann, J. Douglas. Dept. of Neurology, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Diazepam and dialysis encephalopathy.** Neurology. 29(3):414-415, 1979.

A patient with the clinical and electroencephalographic features of dialysis encephalopathy exhibited dramatic improvement with the initiation of diazepam therapy. Although improvement was sustained for a period of several weeks, her clinical condition eventually deteriorated despite continued treatment with diazepam and dialysis. Dialysis encephalopathy in this patient is compared with other cases recently reported in the medical literature as having a similar dramatic response to diazepam. It is concluded that diazepam transiently reverses a component of the dialysis encephalopathy syndrome, but it does not appear to change the ultimate prognosis for patients with this condition. 5 references. (Author abstract)

002737 Solow, Robert A. Division of Scientific and Educational Activities, California Medical Association, 731 Market Street, San Francisco, CA 94103 **Drug treatment of affective illness in children.** Western Journal of Medicine. 129(6):489-490, 1978.

The drug treatment of affective illness in children is discussed. It is suggested that drugs proven to be effective antidepressants in adults have not been well evaluated in depressed children, particularly those with psychomotor retardation. It is argued that symptoms of irritability, excessive crying, fretfulness, and pronounced insomnia are useful criteria for the recognition of endogenous depression in children 1 to 3 years old. This condition and a variety of disorders in older children, in which depression dominates the clinical features, have been treated with tricyclic antidepressants. Imipramine has been administered starting with 10mg and increasing by 10mg every third day until improvement was noted, with 300mg being the maximum dose given. Childhood manic-depressive illness and cyclic alterations of mood that are at a level of clinical significance have been treated with lithium carbonate, as have conditions characterized by rapid shifts in mood, overactivity, and restlessness. It is concluded that lithium is believed to be a safe drug for investigation in children, but is inadequate for treating hyperactivity unresponsive to stimulant medication. 3 references.

002738 Solow, Robert A. Division of Scientific and Educational Activities, California Medical Association, 731 Market Street, San Francisco, CA 94103 **The use of phenothiazines in children.** Western Journal of Medicine. 129(6):489, 1978.

The use of phenothiazines in children is discussed. It is acknowledged that chlorpromazine was the first and initially most widely used phenothiazine in child pharmacology. Indications for thioridazine, another widely used drug, include: agitation,

anxiety, terror and hostility when they are symptoms of psychotic illness, mental retardation, or organic brain damage. Both drugs are widely used in the treatment of autistic children, but because of their sedative effects, they seem to have a negative effect on cognitive behavior and learning. It is contended that both drugs are of value for schoolage schizophrenic children with acute or chronic symptomatology. It is argued that fluphenazine is highly effective in prepubertal autistic schizophrenic children, and that trifluoperazine is better than chlorpromazine in autistic children. It is submitted that drugs should enhance learning and should not be used as chemical straitjackets for psychotic retarded children. It is concluded that abrupt withdrawal of psychotropic drugs causes neurologic withdrawal emergent symptoms, most of which involve involuntary movements in the trunk, head, and ataxia. 3 references.

002739 Solow, Robert A. Division of Scientific and Educational Activities, California Medical Association, 731 Market Street, San Francisco, CA 94103 **Stimulants and hyperkinesis.** Western Journal of Medicine. 129(6):488-489, 1978.

The use of stimulant drugs in the treatment of hyperkinetic children is discussed. It is suggested that drug treatment should be part of a total program for a child, and that consideration must be given to complimentary therapy methods including work with families, suitable programs for the child, educational planning, special groups, and psychotherapy. It is contended that medication should be used when a child with remedial and psychological help continues to show attention difficulty which significantly interferes with his academic or social functioning. It is noted that methylphenidate and dextroamphetamine in hyperactive children causes a highly significant suppression of growth in weight and height, while the long-term use of methylphenidate causes a less striking growth suppression only when daily doses over 20mg are administered. It is concluded that with proper supervision, there is a place for drugs in the treatment of hyperactive children, but that the possibility of unforeseen long-term consequences indicates caution. 3 references.

002740 Stoica, Emilian; Enulescu, Olimpia. Institute of Neurology and Psychiatry, Sos. Berceni 10-12, P.O.B. 5880, R-75622 Bucharest, Romania **Abnormal epinephrine urinary excretion in Parkinsonians: correction of the disorder by levodopa administration.** Journal of the Neurological Sciences (Amsterdam). 38(2):215-227, 1978.

Epinephrine (E) and norepinephrine (NE) as well as vanilmandelic acid (VMA) urinary excretion was investigated in 54 patients with Parkinsonism and 29 controls. In Parkinsonians the mean value of NE excretion was normal, while that of E was significantly higher than in controls. Analysis of results in terms of age showed that only the patients in the 5th and 6th decades displayed significant increases in E excretion when compared to age matched controls. No age group differences were found for NE excretion. VMA was significantly higher in Parkinsonians than in controls. Both in patients and in controls VMA excretion correlated significantly with that of NE, but not with E excretion. Ten day treatment with levodopa of Parkinsonians below the age of 60 was followed by a constant decrease in the excretion of E and a less consistent, nonsignificant increase in the excretion of NE. It is suggested that the adrenal medulla, the main site of E synthesis, may be involved in the pathologic process. 27 references. (Author abstract modified)

002741 Tislow, Richard F.; Skversky, Arleen I.; Santore, Anthony F. Northwestern Institute of Psychiatry, Morris and Lafayette Roads, Fort Washington, PA **The relevance of psychopharmacologic agents for the bereaved in a community mental health center (CMHC).** Archives of the Foundation of Thanatology. 7(1):5, 1978.

In a summary of a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, the use of drug therapy in conjunction with psychotherapy by a community mental health center (CMHC) to aid the bereaved patient was discussed. It was emphasized that the facilities of a CMHC are particularly suited for helping the bereaved for the following reasons: they are accessible to the community, they provide humane care by drug treatment as well as psychotherapy, and they make available a variety of social services beneficial to the bereaved patient. 3 references.

002742 Tourtellotte, Wallace W.; Potvin, Alfred R.; Costanza, Annabelle M.; Hirsch, Sophie B.; Syndulko, Karl. Neurology Service, V.A. Wadsworth Medical Center, Wilshire and Sawtelle Blvds., Los Angeles, CA 90073 **Cyclobenzaprine: a new type of anti-Parkinsonian drug.** Progress in Neuro-Psychopharmacology (Oxford). 2(5/6):553-578, 1978.

The efficacy of cyclobenzaprine (Flexeril) and benzotropine methanesulfonate (Congentin) were assesed in 24 men with Parkinson's desease. A randomized double-blind crossover clinical trial was followed by an extention study with patients permitted to choose either medication. Both medications were judged beneficial to a majority of patients. Of nine evaluation systems used, eight revealed cyclobenzaprine was better, while the ninth indicated that neither drug affected cognition. Differences between the two medications were slight and not significant. In the extension study, 71% of the patients selected cyclobenzaprine and 29% selected benzotropine methanesulfonate. It is suggested that the chemical structure of cyclobenzaprine differs from other antiparkinsonian agents, and this drug may be effective for patients who do not tolerate or benefit appreciably from levodopa or other medicants. 32 references. (Author abstract modified)

002743 Tridon, P.; Mises, R. Clinique de Neuro-Psychiatrie infantile, Institution Jean-Baptiste Thiery, F-54320 Maxeville, France **/Carpipramine in child psychiatry./** La carpipramine en pedopsychiatrie. Encephale (Paris). 4(5, Supplement):587-594, 1978.

In a paper presented at a Conference on the Concept of Inhibition in Psychiatry, Held in Monastir, Yugoslavia, October 1978, an experiment is reported with the use of carpipramine in 35 children and teenagers, most of them suffering from psychosis, which confirms its beneficient action in the majority of those cases. The early observed improvement concerned inhibition, lack of energy, moroseness, favoring the patients' integration in the institutional context. Symptoms of slight excitation are sometimes noted, but they do not always deserve to be called complications, compared to the previous apathy. Tolerance is excellent. The few results obtained in the neurotic and organic symptoms or during hyperkinetic states suggest that longer series should be studied. (Journal abstract modified)

002744 Voinescu, I.; Gheorghita, Natalia. Institute of Neurology and Psychiatry of the Academy of Medical Sciences, Bucharest, Romania **Adjuvant drug therapy with psychologopedic rehabilitation of aphasic patients.** Neurologie et Psychiatrie (Bucuresti). 16(3):155-161, 1978.

Sixty-one aphasics who began treatment with drugs (acetylsalicylic acid, ephedrine, caffeine, pyrithioxine) in conjuction with psychologopedic speech therapy after the spontaneous improvement period had ended, were studied. The results show only pyrithioxine as adjuvant had positive effect as it enhanced the speech therapy. The findings are important especially in severe and very severe aphasia cases in which psychologopedic

therapy alone is insufficient. 20 references. (Author abstract modified)

002745 Vyas, J. N.; Purohit, D. R. Department of Psychiatry, S. P. Medical College, Bikaner (Rajasthan), India **Comparative study of trimipramine with nitrazepam as a hypnotic agent.** Indian Journal of Psychiatry (Poona). 20(3):292-293, 1978.

The comparative efficacy of trimipramine and nitrazepam was evaluated in a sample of 61 psychiatric inpatients complaining of insomnia. Patients were of varying diagnostic classifications including: schizophrenia; involutional, neurotic, secondary, and endogenous depression; hysterical and anxiety neurosis; and puerperal psychosis. Results indicated a therapeutic psychopharmacological response in 74% of patients receiving trimipramine and in 63% of patients in the nitrazepam group; however, the difference was not of statistical significance. Common side-effects included confusion, ataxia, worsening of sleeplessness, and hangover. Depressed and anxious patients responded better to trimipramine than schizophrenics. 3 references. (Author abstract modified)

002746 Warnes, Hector. 197 Cumberland Street, Ottawa KIN 7H4, Ontario, Canada **Premenstrual disorders: causative mechanisms and treatment.** Psychosomatics. 19(1):32-35, 39-40, 1978.

The question of why some women are affected by premenstrual disorders and why some are not was studied in terms of causative mechanisms and treatment. Self-reports and social behavior studies have indicated a behavioral decrement associated with premenstrual and menstrual phases of the cycle in some cases, while other studies have reported premenstrual tension and behavioral changes as primarily physiological in origin, with secondary changes depending on factors of predisposition, autonomic instability, and attitudes. Biochemical studies have shown elevated levels of estrogen and progesterone after ovulation, so that when these are reduced before and during menstruation, depression, anxiety, and irritability will sometimes increase. Women rated low in neuroticism have experimentally demonstrated a consistent mood improvement after the menses and a milder degree of premenstrual tension. Although no consistently effective approach has been found to relieve premenstrual disorders, therapy may be attempted according to predominant changes observed in the patient, e.g.,pharmaceuticals and/or hormones. 39 references. (Author abstract modified)

002747 Weisdorf, Daniel; Kramer, Jeffrey; Goldbarg, Alberto; Klawans, Harold L. Klawans: Dept. of Neurological Sciences, Rush Presbyterian-St. Luke's Medical Center, 1725 West Harrison, Chicago, IL 60612 **Physostigmine for cardiac and neurologic manifestations of phenothiazine poisoning.** Clinical Pharmacology and Therapeutics. 24(6):663-667, 1978.

The use of physostigmine for cardiac and neurological manifestions of phenothiazine poisoning is discussed in relation to a case report of a trifluoperazine overdose. Treatment with physostigmine reversed the central anticholinergic syndrome as well as the electrocardiographic abnormalities. The effects of phenothiazines on altering cardiac status are discussed. 11 references. (Author abstract modified)

002748 Yesavage, Jerome A.; Hollister, Leo E.; Burian, Ernst. Psychiatry Service 116A3, Veterans Administration Hospital, 3801 Miranda Avenue, Palo Alto, CA 94304 **Dihydroergotoxine: 6-mg versus 3-mg dosage in the treatment of senile dementia. Preliminary report.** Journal of the American Geriatrics Society. 27(2):80-82, 1979.

The effects of two dosage levels of dihydroergotoxine mesylate were studied in 14 patients with senile dementia. Only a nonstatistically significant trend was found for superiority of the higher dosage. However, one patient showed remarkable clinical improvement during the 6mg period; the mechanism remains unexplained. Further studies are needed with this higher dosage in less impaired patients and in those with well defined cerebral pathologic changes. 7 references. (Author abstract)

12 PSYCHOTOMIMETIC EVALUATION STUDIES

002749 Koukkou, Martha; Lehmann, D. Research Department, Psychiatric University Hospital, 8029 Zurich, Switzerland **Correlations between cannabis-induced psychopathology and EEG before and after drug ingestion.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 11(5):220-227, 1978.

EEG records were obtained from 12 volunteers before and after oral administration of 200mcg/kg tetrahydrocannabinol (THC). Subjective responses to THC were recorded in self-rating questionnaires. Results indicate that individual differences in responsiveness to THC are systematically correlated with EEG descriptors. The predrug EEG and the resting EEG after THC both had predictive value for body image disturbances and euphoria. Correlations between visual experiences and other psychopathological THC effects with resting EEG descriptors 1 hour after drug ingestion and with EEG changes from the predrug period to 1 hour after ingestion persisted at later times after drug ingestion. These results suggest that interindividual differences in psychophysiological characteristics that influence drug responses are reflected in EEG measures. 30 references. (Author abstract modified)

002750 Leigh, David. no address **LSD: the real risks.** New Society (London). 43(806):606, 1978.

In reference to press publicity surrounding the recent trial a group of dealers in lysergic acid diethylamide (LSD), the risks of LSD use are discussed. It is asserted that dependence potential of LSD is extremely low and physical dependence is nil. While heavy LSD use does not appear to cause brain damage and chromosome damage is no greater than that found with caffeine and aspirin, there is a potential for psychological damage. This, however, appears to be exaggerated: LSD users accounted for only 1% of London drug casualities, and the vast majority of these had used multiple drugs; and drug admissions for LSD were far outnumbered by those for opiates and barbiturates, and slightly less than those for amphetamines. LSD experiments, often involving mental patient subjects, reported a very low incidence of suicide and transient or prolonged psychosis. Compared to other drugs including tobacco and alcohol, LSD related mortalities are very low.

002751 Rhead, John C. Taylor Manor Hospital, Ellicott City, MD 21043 **On the potential utility of nitrous oxide in psychedelic psychotherapy: a pilot study.** Journal of Psychedelic Drugs. 10(2):145-149, 1978.

The potential utility of nitrous oxide in psychedelic psychotherapy was assessed in 10 male and 10 female patients, free from obvious psychopathology, who received nitrous oxide in conjunction with dental treatment. All subjects were administered the Psychedelic Experience Questionnaire (PEQ) and a modified form of the Linton-Langs Questionnaire (LLQ), an instrument which has been used to assess subjective response to psychotomimetics. Data indicated that scores on LLQ and the PEQ tended to be significantly elevated above presumed baseline levels by administration of nitrous oxide in a dental setting. Methodological problems in interpreting these results are discussed. Taken within the context of previous research, however, results suggest the need for further investigation of the utility of nitrous oxide in a psychedelic psychotherapeutic framework. 10 references.

002752 Van Dyke, C.; Jatlow, P.; Ungerer, J.; Barash, P. G.; Byck, R. Dept. of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Oral cocaine: plasma concentrations and central effects.** Science. 200(4338):211-213, 1978.

Plasma concentrations and subjective effects of cocaine following oral and intranasal administration in four male subjects were measured and compared. A 2mg/kg dose of cocaine given orally was found to be at least as effective as the same dose given intranasally. Cocaine was not detected in the plasma until 30 minutes after oral administration, but peak plasma concentrations were similar after both routes. The subjective highs in man were greater after oral than after intranasal administration. 13 references. (Author abstract modified)

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

002753 Bech, Per. Psychochemistry Institute, University of Copenhagen, Rigshospitalet, 9, Blegdamsvej, DK-2100, Copenhagen O, Denmark **Depressive symptomatology and drug response.** Communications in Psychopharmacology (Oxford). 2(5):409-418, 1978.

At the Symposium on the Plasma Level Monitoring of Tricyclic Antidepressants held in Vienna in July 1978, the use of rating scales for measuring depression in antidepressant treatments is discussed. Since different scales are required for different purposes, a multiaxial system of classification based on the therapeutic effects may be useful. The profile of the various antidepressant treatments (ECT, tricyclic drugs, MAO-inhibitors, lithium, REM reduced sleep, and psychotherapy) indicates that multiaxial systems must include: 1) personality variables, 2) symptoms of depression, anger, and anxiety qualitatively different from symptoms of severity, 3) psychogenesis, 4) course, 5) side-effects, and 6) demographic variables. This treatment validated assessment has supported the dichotomy of affective illness into neurotic (depression versus anxiety) and endogenous (unipolar versus bipolar) melancholia. As yet no data seem to indicate differences clinically between the various tricyclic antidepressants. 52 references. (Author abstract modified)

002754 Buchsbaum, Monte S.; Davis, Glenn C. Biological Psychiatry Branch, National Institute of Mental Health, Bethesda, MD 20014 **Application of somatosensory event related potentials to experimental pain and the pharmacology of analgesia. (Unpublished paper).** Bethesda, MD, NIMH, 1978. 12 p.

In order to help clarify analgesic effects, experiments with aspirin were conducted and different techniques of evoked potential (EP) processing and peak measurements were compared. Forty-seven normal adult volunteers participated in a test/retest reliability study and 32 in a double-blind crossover study of aspirin. Aspirin was found to diminish the EP amplitude. Individual differences in analgesic effects were reflected in significant correlations between the magnitude of the changes associated with aspirin in psychophysical and EP measures. The analgesia associated with aspirin appeared distinct in origin from that found with physostigmine. The greater specificity of the EP measures as opposed to psychophysical measures, combined with its reliability, suggests the utility of somatosensory EP recordings in psychopharmacological investigations. 14 references.

002755 Carl, G. F.; Benesh, F. C.; Hudson, J. L. Department of Psychiatry, Neurosciences Program, Medical Center, University of Alabama, Birmingham, AL 35486 **Effect of methionine-loading on methyl group synthesis and activation in rat brain and liver.** Biological Psychiatry. 13(6):661-669, 1978.

The effect of methionine loading on methyl group synthesis and activation was investigated in rat brain and liver. Much greater increases in S-adenosylmethionine (SAM) concentrations were observed in the liver in response to methionine loading than in the brain due to differences in the methionine adenyltransferase (MAT) activities in these tissues. Live MAT exhibited a bimodal saturation curve with a nonlinear Lineweaver-Burk plot, indicating that high methionine concentrations are required for saturation. In the brain, MAT was saturated in vitro at a methionine concentration less than the normal physiological concentration. Increased SAM concentrations in liver of methionine treated rats also accounted for the observed inhibition of N5,N10-methylenetetrahydrofolate reductase activity in this tissue. No inhibition of this enzyme was observed in the brain of methionine treated animals, nor were SAM concentrations increased significantly in brain. Serine hydroxymethyltransferase activity responded to methionine loading by decreasing in brain and increasing in liver. Findings are discussed in relation to the hypothesized undermethylation in some schizophrenics. 29 references. (Author abstract modified)

002756 Chapman, C. R.; Benedetti, C. University of Washington, Seattle, WA 98195 **Reversal of analgesia with naloxone as measured by cortical evoked potentials.** Psychophysiology. 15(3):287-288, 1978.

A summary is presented of a report on the effects of various analgesics on cortical evoked potentials (EPs) to tooth pulp shock in three groups of subjects treated with transcutaneous electrical stimulation (TES), electrical acupuncture, and 0.1mg fentanyl and naloxone employed to reverse the analgesic states, which was delivered to the Seventeenth Annual Meeting of the Society for Psychophysiological Research, held in Philadelphia, October 1977. EPs were assessed before and after analgesia and following administration of naloxone. Analgesic treatments produced significant reductions in EP amplitude in all three groups. Amplitude recovered following naloxone injection only in the fentanyl group. The findings demonstrate, that evoked potential responses to tooth pulp shock are a potentially powerful way to measure analgesic states, although changes in the evoked response may not necessarily reflect analgesia. (Author abstract modified)

002757 Cianchetti, C.; Masala, C.; Corsini, G. U.; Mangoni, A.; Gessa, G. L. Institute of Neurology, University of Cagliari, Italy **Effect of apomorphine on human sleep.** Life Sciences. 23(4):403-408, 1978.

The effect of intravenous infusion ofapomorphine in nonemetic doses (10 to 15 /min) on the sleep of 10 Ss was determined to further clarify the specific role of dopamine (DA) in human& sleep regulation and the overall role of brain catecholamines in regulating the sleep wakefulness mechanisms in man. Apomorphine was used because it is a direct stimulant of DA receptors. During apomorphine infusion for 180 min, a complete suppression of REM sleep and a dramatic reduction of the amount of delta sleep occurred. The EEG pattern was thus characterized almost exclusively by the presence of light sleep. After discontinuance of apomorphine, a rebound increase in REM sleep occurred. Results support the contention that brain catecholamines, in general, and DA, in particular, exert an inhibitory affect on REM and delta phases of human sleep. 20 references. (Author abstract modified)

002758 Consbruch, U.; Degkwitz, R.; Koufen, H. Koufen: Univ.-Nervenklinik, Hauptstrasse 5, D-7800 Freiburg, Germany **/Lithium balance in healthy volunteers./** Untersuchungen zur Lithiumbilanz bei gesunden Probanden. Pharmakopsychiatrie/ Neuro-Psychopharmakologie (Stuttgart). 11(5):228-234, 1978.

Lithium balance was studied in three healthy volunteers given a sustained release preparation of lithium sulphate for 10 days.

Effective serum lithium levels (0.7-0.8mmol/1) could be maintained with a daily dose of 30mval lithium. A steady state serum lithium concentration was achieved after 4 to 5 days. The mean value of lithium clearance was 26.8ml/minute. About 98% of the ingested lithium was recovered from the urine. Six days after drug withdrawal, no lithium was detected in serum or urine. Results indicate that lithium balance can be determined solely on the basis of renal excretion. The effect of simultaneous ingestion of psychotropic drugs and sodium chloride on the elimination of lithium is discussed. 26 references. (Author abstract modified)

002759 Costa, Jonathan L.; Kirk, Kenneth L. Clinical Neuropharmacology Branch, NIMH, Bethesda, MD 20014 **Re-evaluation of the uptake of desoxyfructo-serotonin by human platelets, and of its effect on the uptake of serotonin. (Unpublished paper).** Bethesda, MD, NIMH, 1978. 7 p.

C14-glucose and C14-serotonin (5-hydroxytryptamine, 5HT) were used as precursors in the synthesis of desoxyfructo-5HT(1-desoxy-1-(5-hydroxytryptamine)-D-fructose) labelled either in the sugar or 5HT moieties, and the uptake of the labelled substrate by washed human platelets was examined. Desoxyfructo-5HT appeared to interact with the 5HT uptake site, effectively inhibiting the uptake of H3-5HT. However the data indicate that, contrary to published reports, the entry of desoxyfructo-5HT into platelet vesicles or cytoplasm is negligible. 11 references. (Author abstract)

002760 Dehen, H.; Willer, J. C.; Prier, S.; Boureau, F.; Cambier, J. Clinique Neurologique, Hopital Beaujon, 100 Bd. General Leclerc, F-92110 Clichy, France **Congenital insensitivity to pain and the ""morphine-like" analgesic system.** Pain (Amsterdam). 5(4):351-358, 1978.

The relationship between congenital insensitivity to pain and an hyperactivity of a naturally occurring morphine-like pain inhibitory system was investigated. In an electrophysiological study on a nociceptive flexion reflex of the lower limb, the effects of naloxone and of placebo were compared in eight normal Ss and in a patient with congenital insensitivity to pain. In normal Ss, no significant change in the reflex threshold was observed with naloxone or with placebo. In contrast, two electrophysiological abnormalities characterized the patient: 1) spontaneous elevation in the nociceptive reflex threshold of 350% as compared to control, and 2) a large (67%) and rapid (2 to 3 min.)fall of this threshold for about 10 min following the administration of naloxone. 34 references. (Author abstract modified)

002761 DiGregorio, G. John; Piraino, Anthony J.; Ruch, Eileen. Dept. of Pharmacology, Hahnemann Medical College, 230 N. Broad Street, Philadelphia, PA 19102 **Diazepam concentrations in parotid saliva, mixed saliva, and plasma.** Clinical Pharmacology and Therapeutics. 24(6):720-725, 1978.

The concentration of diazepam in the plasma and saliva of nine normal human Ss receiving a single oral dose of diazepam (10mg) over an 8 hr period was determined by gas liquid chromatography/electron capture analysis; and the binding of diazepam to plasma protein in these Ss was determined using equilibrium dialysis at specific time intervals corresponding to periods of plasma and saliva collection. A linear relationship was found between diazepam concentration in plasma and that in both mixed and parotid saliva. Results indicate that there is no significant difference between parotid saliva and mixed saliva concentrations over a period of 8 hr after a single oral dose of diazepam. The appearance of diazepam in saliva may provide an alternative, noninvasive method of determining plasma diazepam levels. 13 references. (Author abstract modified)

002762 Edwards, David J.; Antelman, Seymour M. Dept. of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213 **Monoamine oxidase and the metabolism of phenylethanolamine, tyramine and octopamine. (Unpublished paper).** Research Report, NIMH Grants MH-24114 and MH-28340, 1978. 32 p.

The literature on monoamine oxidase (MAO) is reviewed: multiple forms of MAO are discussed, the metabolism of tyramine (TA), octopamine (OCT), and phenylethanolamine (PEOH) by MAO is reviewed, and abnormalities in the metabolism of the trace amines in clinical disorders are examined. The literature shows that the existence of two forms of MAO in mammalian tissues is well established; however, it is still possible that there are subtypes of either type-A, type-B, or both forms of MAO. It is concluded that whereas the phenolic amines including TA and OCT are substrates for both type-A and type-B forms of MA, the ring unsubstituted amines (that is, PEOH and phenylethylamine) are selective substrates for type-B MAO. The physiological consequences which can be attributed to alterations in the metabolism of these amines through changes in MAO activity caused by either drug therapy or disease states (phenylketonuria, hypertyrosinemia, Parkinson's disease, schizophrenia, and affective disorders) remain to be determined. 97 references.

002763 Evrard, J.-L.; Baumann, P.; Pera (-Bally), R.; Peters-Haefeli, L. Lab. de biochimie, Clinique Psychiatrique Universitaire de Lausanne, CH-1008 Prilly, Switzerland **Lithium concentrations in saliva, plasma and red blood cells of patients given lithium acetate.** Acta Psychiatrica Scandinavica (Kobenhavn). 58(1):67-79, 1978.

Lithium concentrations in saliva, plasma and red blood cells were measured in six hospitalized patients under long-term lithium therapy at 2, 5, 9, 12, and 24 hours, after oral doses of lithium acetate and on 10 outpatients under chronic lithium treatment at two occasions 8 days apart. With changing plasma concentrations, saliva lithium varied without any notable time lag. Saliva lithium was always much higher than plasma lithium. Lithium concentrations in red blood cells were always lower than in plasma, and lagged considerably behind plasma changes during changing plasma concentrations. Prediction of plasma lithium concentration from measured saliva lithium appears hazardous, and may provide reliable indications only if saliva lithium is measured repeatedly. 18 references. (Author abstract modified)

002764 Forsman, Anders O. Lollhagen Hospital, Gothenburg, Sweden **/Individual variability in response to haloperidol./** Variabilidad individual en la respuesta al Haloperidol. Acta Psiquiatrica y Psicologica de America Latina (Buenos Aires). 24(2):149-153, 1978.

The individual differences in the clinical effect of haloperidol were examined. To determine the precise nature of individual variability in response to haloperidol, the concentration of the drug at the site of action was studied using a gaseous chromatograph. The drug was administered orally in one group of patients and intravenously in the other. The results show that individual biodispensability, volume of distribution, and capacity for metabolism of the drug all affect the response to the drug. The implications for haloperidol metabolism and excretion are discussed. 11 references.

002765 Garland, W. A.; Min, B. H.; Birkett, D. J. Dept. of Biochemistry and Drug Metabolism, Hoffmann-La Roche Inc., Nutley, NJ 07110 **The kinetics of amitriptyline following single oral dose administration to man.** Research Communications in Chemical Pathology and Pharmacology. 22(3):475-484, 1978.

Amitriptyline and its metabolite, nortriptyline, were studied in the plasma of eight humans for 96 hours following oral administration of a 75mg dose of amitriptyline hydrochloride. Based on the 24 to 96 hour concentration data, the apparent terminal half time of nortriptyline was 26 hours for seven Ss. For these same seven Ss, the relative area under the plasma concentration time curve of nortriptyline was only .88 times that of amitriptyline. One S whose apparent nortriptyline half time was 108 hours had a nortriptyline bioavailability 3.83 times that of amitriptyline. Average steady state plasma levels for 12 psychiatric patients who had received a 50mg oral dose of amitriptyline three times a day for an average of 32 days could be predicted from the single dose plasma clearance of amitriptyline. 18 references. (Author abstract modified)

002766 Gillin, J. C.; Sitaram, N.; Mendelson, W. B.; Buchsbaum, M. S.; Moore, A. M.; Jacobs, L. S.; Wyatt, R. J. Adult Psychiatry Branch, DCBR, IRP, NIMH, Bethesda, MD 20014 **Cholinergic modulation of sleep, growth hormone and analgesia in normal volunteers.** In: Jenden, D., Cholinergic mechanisms and psychopharmacology. New York, Plenum, 1978. 885 p. Vol. 24 (p. 781-789).

At the third Symposium on Cholinergic Mechanisms and Psychopharmacology, held in La Jolla, CA, March 1977, a paper summarizing investigations on cholinergic mechanisms in the induction of rapid eye movement (REM) sleep, arousal, pain, and plasma concentrations of growth hormone was presented. To test the hypothesis that cholinergic mechanisms trigger or maintain REM sleep and arousal, the effects of physostigmine and placebo were compared in human volunteers. Data indicate that physostigmine induced either REM sleep or arousal, depending on the dose and time of the infusion. To determine whether the psychological aspects of the physostigmine-induced REM sleep were normal, the same experiment was repeated and subjects were awakened out of REM sleep. When comparing the dreams reported after physostigmine-induced REM sleep with those reported after spontaneous REM sleep, subjects reported equally vivid dreams. To assess the involvement of cholinergic mechanisms with plasma concentration of growth hormone during sleep, methscopolamine was administered by intramuscular injection into volunteers. The blood sampled indicates that methscopolamine significantly blocked the release of growth hormone during sleep, but did not alter sleep patterns. These experiments suggest that cholinergic mechanisms are involved in a number of normal physiological and psychological processes in humans.

002767 Ginestet, D. Service de Neuropsychiatrie, 1, rue Richaud, Hopital de Versailles, F-78000 Versailles, France **/Disinhibitory neuroleptics./** Neuroleptiques desinhibiteurs. Encephale (Paris). 4(5, Supplement):541-545, 1978.

In a paper presented at the Conference on the Concept of Inhibition in Psychiatry, held in Monastir, Yugoslavia, October 1978, the use of neuroleptic disinhibitors in psychiatry is discussed. It is noted that the concept of disinhibition appeared in 1956 (Broussolle and Dubor) with a study of the activity of prochlorpemazine in chronic schizophrenia. Each chemical group of neuroleptics includes at least one or two disinhibitory compounds. This activity intervenes upon the affective and intellectual life without necessarily producing the usual extrapyramidal akathic side-effects. It is concluded that neuroleptics can have a favorable and prolonged but inconsistent effect on disinhibition, so accompanying psychotherapy and sociotherapy are advisable. 7 references. (Journal abstract modified)

002768 Goetz, Christopher G.; Weiner, William J. Dept. of Neurological Sciences, Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL 60612 **Huntington's disease: current concepts of therapy.** Journal of the American Geriatrics Society. 27(1):23-26, 1979.

Current concepts concerning the genetic disease Huntington's disease or Huntington's chorea are reviewed. Since there is no cure, therapy has focused on pharmacologic manipulation of the involved neurotransmitter systems. In Huntington's disease there is a functional predominance of striatal dopaminergic activity over antagonist cholinergic and possibly gamma-aminobutyric acid (GABA)-minergic systems. Many dopaminergic antagonists and cholinergic and GABA-minergic agonists are currently used in treatment. Supportive psychiatric care for affected persons and their families is also an important therapeutic device in the management of the disease. It is concluded that the eventual care will depend upon accurate identification of the primary genetic defect. 30 references. (Author abstract)

002769 Greenblatt, David J.; Shader, Richard I. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **Pharmacokinetic understanding of antianxiety drug therapy.** Southern Medical Journal. 71(2):2-9, 1978.

Pharmacokinetic characteristics of benzodiazepine antianxiety agents were reviewed and differences in patterns of absorption, distribution, and elimination by the human body were examined in a paper presented at the McLean Hospital Symposium held in Dallas, November 1977. The specific antianxiety agents chlordiazepoxide, diazepam, chlorazepate, prazepam, lorazepam, and oxazepam are discussed. It is suggested that the longer acting compounds are suitable for once daily administration, since considerable drug accumulation occurs and leads to persistence of the drug. With shorter acting compunds, drug accumulation is not extensive, and cumulative sedative effects are seldom a problem. It is concluded that the pharmacokinetics of each benzodiazepine derivative confer certain potential advantages as well as disadvantages, depending on the needs of the individual patient. 45 references.

002770 Halberg, F. Chronobiology Laboratories, University of Minnesota, Minneapolis, MN 55455 **The chronobiology of convulsive disorders with notes on drugs affecting the C.N.S.** Totus Homo (Milano). 8(1-2-3):20-30, 1978.

Findings since the early 1900s on the chronobiology of convulsive disorders are reviewed and notes about some drugs affecting the central nervous system are presented. Studies have concerned classification of epileptics according to the time of day when most seizures occur, the time distribution of seizures, the change in periodicity of seizures induced by drugs, the relationship between the rhythm in EEG pathology and sleep or lack of sleep rhythms, and the effect of hormonal changes and seizures. It is suggested that an exclusive focus on sleep be abandoned in dealing with convulsive periodicity and that modern methods of microscopic rhythmometry be used to analyze the component in the EEG and in other physiologic functions, including hormones in blood and urine, in order to see which are coupled, which can be separated in health, and which are modified in different kinds of disease. 56 references.

002771 Holmes, J. H.; Kanfer, I.; Zwarenstein, H. Dept. of Pharmacology, Medical School, University of Cape Town, Observatory 7925, Cape Town, South Africa **Effect of benzodiazepine derivatives on purified blood cholinesterases in vitro.** Research Communications in Chemical Pathology and Pharmacology. 22(2):431-432, 1978.

The in vitro effect of several benzodiazepine derivatives on purified blood cholinesterases were determined and compared with results obtained on freshly drawn human blood. The cholinesterases used in these experiments were purified preparations from human serum and from bovine erythrocytes. Results ob-

tained with the purified human serum cholinesterase preparation were in excellent agreement with those obtained using human plasma. The results on the red cell enzyme were not in such close agreement. 1 reference. (Author abstract modified)

002772 Iversen, Leslie L. MRC Unit of Neurochemical Pharmacology, Cambridge, England **GABA and benzodiazepine receptors.** Nature (London). 275(5680):477, 1978.

Research on gamma-aminobutyric acid (GABA) and benzodiazepine receptors is reviewed. A series of recent studies which are reported suggests that some interaction may exist between the two types of receptors. It is suggested that benzodiazepines might act normally to enhance the actions of GABA at its receptors by displacing an endogenous modulator protein which forms part of a macromolecular complex constituting the GABA receptor ionophore. Some discussion is given to the cellular localization and molecular nature of the benzodiazepine receptors, but knowledge in this area remains limited.

002773 Javaid, J. I.; Fischman, M. W. Schuster, C. R.: Dekirmenjian, H.; Davis, J. M. Illinois State Psychiatric Institute, Chicago, IL 60612 **Cocaine plasma concentration: relation to physiological and subjective effects in humans.** Science. 202(4364):227-228, 1978.

A correlation of physiological and subjective effects with plasma concentration of cocaine in the same subjects is presented. Ten volunteer subjects with previous histories of cocaine use were administered cocaine hydrochloride intravenously or intranasally. There was a positive relationship between peak plasma concentrations, physiological and subjective responses, and dose administered. The rate of cocaine disappearance after intravenous administration paralleled the drop in physiological and subjective drug effects. After intranasal administration, blood levels remained elevated for a considerably longer time. Data suggest that in subjects showing an initial response to cocaine administration, compensatory mechanisms are triggered which result in a faster decline of both cardiovascular and subjective effects than of plasma cocaine concentration. 7 references. (Author abstract modified)

002774 Johansson, Barbro B. Dept. of Neurology, University of Goteborg, Sahlgren Hospital, S-413 45 Goteborg, Sweden **Effect of beta-adrenoreceptor antagonists on the increased cerebrovascular permeability to protein induced by amphetamine.** Progress in Neuro-Psychopharmacology (Oxford). 2(5/6):529-534, 1978.

The effect of various beta receptor blocking drugs on the amphetamine-induced blood brain barrier dysfunction was examined to study which type of beta receptors might be predominantly involved in the effect of amphetamine on cerebral circulation. It was found that leakage of 125I-serum albumin after amphetamine administration could significnatly be reduced by d,1-propranolol and beta2-adrenoreceptor antagonists but not by d-propranolol and betal-antagonists. The difference could not be explained from blood pressure levels. A likely explanation is that vasodilation was prevented in rats given nonselective and beta2-selective antagonist. It is suggested that as the beta-adrenoreceptors in cerebral vessels are of the betal type, it is likely that the antagonists act predominantly on intracerebral receptors. 30 references. (Author abstract modified)

002775 Kelly, John G.; O'Malley, Kevin. Dept. of Clinical Pharmacology, Royal College of Surgeons in Ireland, St. Stephen's Green, Dublin 2, Ireland **Plasma concentrations of drugs as a guide to therapy in clinical practice.** Journal of the Irish Medical Association (Dublin). 71(17):578-582, 1978.

Plasma concentrations of drugs are discussed as a guide to clinical therapy. Measurements of blood concentrations can be useful either to increase the effectiveness of therapy or to minimize toxic effects. A good correlation between concentration and effect will be found in drugs which show a reversible competitive interaction with their receptors; if tolerance does not develop; if active metabolites are not responsible for a significant part of the measured drug effect; and when the concentration of nonprotein bound drug in plasma reflects the concentration of unbound drug at receptors. Protein binding of drugs is discussed, and procedures for sampling drug concentrations are outlined. Monitoring of plasma drug concentrations is discussed in terms of the pharmacokinetics of a variety of drugs including lithium, and a listing of known therapeutic ranges for a number of drugs is provided. 22 references.

002776 Kopera, H. Institut f. Exper. u. Klin. Pharmakologie d. Universitat Graz, Universitatsplatz 4, A-8010 Graz, Austria **Cardiovascular tolerance of mianserin and interactions of mianserin with other drugs.** Acta Psychiatrica Belgica (Brussels). 78(5):787-797, 1978.

Data are presented which indicate that mianserin, which is therapeutically equal to other antidepressants, is a drug with a new chemical structure and a different biochemical mechanism of action. Distinct advantages over comparable compounds are evident. Mianserin not only has clearly fewer anticholinergic and central side-effects, but also has no apparent cardiotoxic effects on healthy or depressed individuals or on cardiac patients. It does not cause orthostatic hypotension and is devoid of adverse drug/drug interaction with coumarin-like anticoagulants, with sympathomimetic amines, and with antihypertensive agents. The drug exhibits few and short lasting interactions with alcohol. 19 references. (Journal abstract modified)

002777 Korczyn, Amos D. Department of Neurology, Mount Sinai Medical School, New York, NY 10029 **Mechanism of placebo analgesia.** Lancet (London). 2(8103):1304-1305, 1978.

Dr. Jon Levine's study suggesting that naloxone, a specific narcotic antagonist, reverses placebo analgesia is criticized. Rather than comparing pain rating changes after placebo given at D1 with pain rating changes after naloxone given at D1, the data given reveals the effects of placebo versus naloxone given at D2 to patients given placebo at D1. It is further argued that the data presented is unclear, incomplete, and given erroneously. 3 references.

002778 Kragh-Sorensen, Per. Odense University Hospital, DK-5000 Odense C, Denmark **Correlation between plasma levels of nortriptyline and clinical effects.** Communications in Psychopharmacology (Oxford). 2(5):451-456, 1978.

At the Symposium on Plasma Level Monitoring of Tricyclic Antidepressants held in Vienna in July 1978, the correlation between plasma levels of nortriptyline and clinical effects studied in eight experiments was reported. Evidence indicates that the best therapeutic result is obtained within a range of 50 to 150ng/ml. Side-effects, specifically severe ECG changes, were observed above 200ng/ml. The practical significance of these findings are analyzed. 21 references. (Author abstract modified)

002779 Lee, Tyrone; Seeman, Philip; Tourtellotte, W. W.; Farley, Irene J.; Hornykeiwicz, Oleh. Dept. of Pharmacology, University of Toronto, Toronto M5S 1A8, Canada **Binding of 3H-neuroleptics and 3H-apomorphine in schizophrenic brains.** Nature (London). 274(5674):897-900, 1978.

In a study of the binding of 3H-haloperidol, 3H-spiperone, and 3H-apomorphine to four regions of postmortem brains from schizophrenic patients, direct evidence for brain dopamine re-

ceptor abnormalities in schizophrenia is described. A total of 28 neurologically normal and 20 schizophrenic postmortem brains were analyzed. There was no difference between normal and schizophrenic brains for 3H-apomorphine, yet there was a significantly higher amount of specific 3H-haloperidol binding in the three main dopamine rich regions of the schizophrenic brains (caudate, putamen, and nucleus accumbens). The implications of these results for the dopamine hypothesis of schizophrenia are unclear; however, the results support the notion that neuroleptic-induced tardive dyskinesia may stem from a drug-induced increase in dopaminergic sensitivity. 27 references.

002780 Lerner, Pauline; Goodwin, Frederick K.; van Kammen, Daniel P.; Post, Robert M.; Major, L. Franklin; Ballenger, James C.; Lovenberg, Walter. Biological Psychiatry Branch, National Institute of Mental Health, Bethesda, MD 20014 **Dopamine-beta-hydroxylase in the cerebrospinal fluid of psychiatric patients.** Biological Psychiatry. 13(6):685-694, 1978.

The activity of dopamine-beta-hydroxylase (DBH) in cerebrospinal fluid (CSF) from 59 psychiatric patients was analyzed by a highly sensitive radioenzymatic assay. There was no sex difference in DBH, but there was a significant positive correlation with age. Probenecid administration had no effect on CSF DBH. DBH in CSF correlated positively with the plasma enzyme. Among patients hospitalized for personality disorders, major depressive disorder, unipolar or bipolar schizoaffective disorder, schizophrenia, or alcoholism, there were no significant differences between groups. Among patients with bipolar affective disorder, DBH activity in manic patients was significantly lower than that from depressed or euthymic patients. Results are discussed with reference to the theory that the amount of DBH in CSF may serve as an indicator of central noradrenergic activity. 27 references. (Author abstract)

002781 Levine, Jon D.; Fields, Howard L. Departments of Neurology and Physiology, University of California School of Medicine, San Francisco, CA 94143 **Mechanism of placebo analgesia.** Lancet (London). 2(8103):1305, 1978.

Responses to criticisms made by Dr. Amos Korczyn of a study on the mechanism of placebo analgesia are presented. He argues that study design, division of patients into placebo reactors and nonreactors, and time measurements are not valid and this is contradicted. It is maintained that the observation that placebo reactors showed a much greater increase in pain than did nonreactors when naloxone was given supports the study's conclusion that naloxone reverses placebo analgesia. 4 references.

002782 Levine, Jon D.; Gordon, Newton C.; Fields, Howard L. Department of Neurology, University of California, San Francisco, CA 94143 **The mechanism of placebo analgesia.** Lancet (London). No. 8091:654-657, 1978.

The effect of naloxone on dental postoperative pain was studied to examine the hypothesis that endorphins mediate placebo analgesia. All patients had extraction of impacted mandibular third molars with diazepam, nitrous oxide, and local block with mepivacaine. Three and four hours postsurgery naloxone or a placebo was given under randomized, double-blind conditions, and pain was evaluated on a visual analogue scale. Patients given naloxone reported significantly greater pain than those given placebo. It is concluded that enhancement of reported pain produced by naloxone can be entirely accounted for by its effect on placebo responders. 28 references. (Author abstract modified)

002783 Linnoila, M.; Lamberg, B.-A.; Seppala, T.; Karonen, S.-L. Dept. of Pharmacology, University of Helsinki, Helsinki, Finland **Combined effect of pimozide and thyroliberin (TRH) on serum prolactin and thyroid stimulating hormone (TSH) in man.** Acta Pharmacologica et Toxicologica (Kobenhavn). 43(1):72-74, 1978.

The interaction of pimozide and thyroliberin (TRH) on serum prolactin levels (SPRL) and thyroid stimulating hormone (TSH) in healthy volunteers was investigated. It was hypothesized that the effects of these agents on SPRL would be additive and no effect of pimozide on the TRH-induced TSH response was expected. As hypothesized, TRH induced a significant and normal TSH and SPRL response in every Ss after placebo. Pimozide increased SPRL more than 10ng/ml in three Ss; pimozide reduced the TRH-induced SPRL increases more than 10ng/ml in another three Ss. Results suggest that the pimozide-induced and TRH-induced SPRL increases are due to different mechanisms of actions.

002784 Lund, J.; Christensen, J. A.; Bechgaard, E.; Molander, L.; Larsson, H. Research Laboratory, A/S Ferrosan, DK-2860 Soborg, Denmark **Pharmacokinetics of femoxetine in man.** Acta Pharmacologica et Toxicologica (Kobenhavn). 44(3):177-184, 1979.

The pharmacokinetics of femoxetine, structurally new 5-hydroxytryptamine inhibitor with antidepressant properties, were investigated in seven healthy male volunteers. Femoxetine was almost completely absorbed after an oral dose, but only 5-10% reached the systemic circulation due to extensive first pass metabolism. The metabolites had distributions and excretion rates similar to those of the parent compound. Only a small part (less than 2%) was excreted as femoxetine in the urine. The urinary excretion of the parent compound varied more than 100-fold, depending in the pH of the urine. Most of the substance (up to 80%) was eliminated by urinary excretion of metabolites, and only a small part of a radioactive dose of femoxetine (up to 11%) was excreted in the feces. The pharmacokinetic parameters did not appear to be dose dependent over the range examined, but it was not possible to determine if bioavailability was dependent on the dose. 22 references. (Author abstract modified)

002785 Magnussen, I.; Engbaek, F. University Dept. of Neurology, Aarhus, Denmark **The effects of aromatic amino acid decarboxylase inhibitors on plasma concentrations of 5-hydroxytryptophan in man.** Acta Pharmacologica et Toxicologica (Kobenhavn). 43(1):36-42, 1978.

The effect of aromatic amino acid decarboxylase inhibitors on the accumulation and elimination of 5-hydroxytryptophan (5-HTP) in plasma was studied in five Ss. The plasma concentrations of 5-HTP were increased about 10 fold by pretreatment with the decarboxylase inhibitors, carbidopa and benserazide. Half lives of 2.2to 3.0hours were obtained following oral administration of a single dose of 5-HTP with or without pretreatment. In one S, the half life of 5-HTP in plasma increased to 5.5hours during long-term treatment with carbidopa. 19 references. (Author abstract modified)

002786 Majumdar, Sisir K.; Shaw, G. K.; Thomson, Allan D. Bexley Hospital, Kent, England **Effect of chlormethiazole on serum prolactin.** British Medical Journal (London). No. 6147:1266-1267, 1978.

The effect of chlormethiazole, a central nervous system depressant used in the treatment of anxiety/tension states, psychomotor agitation, and sleep disturbance, on serum prolactin levels was evaluated in 16 male chronic alcoholics. Results indicated that mean serum prolactin levels fell from 281.9mU/1 (or - 19.9) to 174.4mU/1 (or - 15.5) during the course of treatment. The possibility that chlormethiazole interferes with the intrahypothalamic neurotransmitters (dopamine and serotonin) that reg-

ulate prolactin release and/or secretion, is suggested. 4 references.

002787 Martin, Joseph B.; Tolis, George; Woods, Ivan; Guyda, Harvey. Dept. of Neurology, Massachusetts General Hospital, Fruit Street, Boston, MA 02114 **Failure of naloxone to influence physiological growth hormone and prolactin secretion.** Brain Research (Amsterdam). 168(1):210-215, 1979.

The effects of naloxone on growth hormone (GH) and prolactin (PRL) secretion were examined in freely moving male CD rats and in five women during sleep. Administration of naloxone (0.4, 10, or 20mg/kg iv) had no effect on GH or PRL in rats. Naloxone also failed to influence nocturnal GH or PRL secretion in the human subjects; the opiate antagonist had no effect on total sleep time or sleep stages in these Ss. Results indicate that endogenous opioids have a minor role, if any, in the mediation of physiologic GH and PRL secretion. 23 references.

002788 Mendelson, Wallace B.; Jacobs, Laurence S.; Gillin, J. Christian; Wyatt, Richard J. Laboratory of Clinical Psychopharmacology, SMR, IRP, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Regulation of sleep-related growth hormone and prolactin secretion. (Unpublished paper).** Washington, DC, NIMH, 1978. 1 p.

Pharmacologic manipulation of sleep related growth hormone (GH) and prolactin (PRL) secretion as it relates to the roles of the serotonergic, noradrenergic, and cholinergic systems in anterior pituitary regulation is discussed. The serotonin receptor blocker methysergide was administered for 48 hours to normal young adults. Administration was associated with an increase in several measures of sleep related GH secretion. Another experiment showed that a single IM injection of the anticholinergic agent methscopolamine profoundly suppressed sleep related GH secretion. It is concluded that: 1) serotonergic mechanisms may have an inhibitory role, and cholinergic mechanisms may have a facilitory role, in regulation of sleep related GH secretion; and 2) data drawn from pharmacologic manipulation of daytime insulin provocative testing may lead to erroneous conclusions regarding physiologic control of GH secretion. (Author abstract modified)

002789 Merory, J.; Du Boulay, G. H.; Marshall, John; Morris, Jacqueline; Ross Russell, R. W.; Symon, Lindsay; Thomas, D. J. University Dept. of Clinical Neurology, The National Hospital, Queen Square, London WC1N 3BG, England **Effect of tinofedrine (Homburg D8955) on cerebral blood flow in multi-infarct dementia.** Journal of Neurology, Neurosurgery, and Psychiatry (London). 41(10):900-902, 1978.

Tinofedrine (Homburg D8955), a new derivative of l-norephedrine, was examined for cerebral vasodilator activity in 10 patients with reduced cerebral blood flow (CBF) and multiinfarct dementia. Intravenous administration of tinofedrine resulted in significant increases in CBF (by 28%). CBF was measured by noninvasive isotopic clearance technique using the bicompartmental analysis of Obrist et al (1975). 9 references. (Author abstract modified)

002790 Miley, Dennis P.; Abrams, Alan A.; Atkinson, J. Hampton; Janowsky, David S. Department of Psychiatry, University of California, San Diego, School of Medicine, La Jolla, CA 92037 **Successful treatment of thalamic pain with apomorphine.** American Journal of Psychiatry. 135(10):1230-1232, 1978.

The effects of apomorphine, a dopamine receptor agonist, on thalamic pain were tested. Two case reports are presented. Because of evidence suggesting a role for dopamine as a moderator of analgesia and pain perception, it was hypothesized that apomorphine has analgesic properties. In the two cases, intractable pain was successfully moderated by apomorphine where a number of other approaches had failed. The trial of other treatment modalities eliminated the placebo effect as an explanation. 10 references.

002791 Minami, Katsumasa. Department of Neuropsychiatry, Kansai Medical University, Osaka, Japan **A study on quantification of EEG changes induced by psychotropic drugs.** Psychiatria et Neurologia Japonica (Tokyo). 80(7):351-382, 1978.

Induced changes in scalp recorded EEGs after 1, 3, and 6 hours were examined in 14 normal male volunteers. Eight subjects were orally administered inert placebo and 2mg diazepam and six Ss were administered inert placebo and 25mg imipramine. EEGs were recorded under reaction time measurements using two different tone stimuli given in a randomized order at random intervals to protect the subjects from drowsiness. The EEG recordings were later analyzed with digital and hybrid zero cross methods and power spectra technic. The predrug EEG presented normal frequency histograms, but with certain individual differences. Group profiles representing EEG changes after the inert placebo showed a significant increase of slow waves and decrease of fast activity, which seemed to result from reduction of psychic tension. Individual profiles showed marked individual differences. Diazepam produced a decrease of slow waves associated with increases of alpha and 20.1-26.6Hz fast activity in group profiles as well as in individual profiles, but there were less marked individual differences than with inert placebo. Imipramine produced a significant decrease of alpha activity and increases of slow and fast waves, but individual differences were minimal. 52 references. (Author abstract modified)

002792 Mohler, H.; Okada, T. Pharmaceutical Research Dept., F. Hoffmann-La Roche, Basel, Switzerland **The benzodiazepine receptor in normal and pathological human brain.** British Journal of Psychiatry (London). 133(September):261-268, 1978.

The role of the benzodiazepine receptor in normal and pathological human brain tissue is discussed in a paper addressed to the Annual Meeting of the British Association for Psychopharmacology held on April 7, 1978. Benzodiazepines bind with high affinity to a specific benzodiazepine receptor, which occurs exclusively in the central nervous system. The affinity of various benzodiazepines to the receptor closely parallels their pharmacological and therapeutic potency. In Huntington's chorea a decrease in benzodiazepine receptor binding is found in caudate nucleus and putamen, which, at least in putamen, is due to a loss of benzodiazepine receptors apparently located on gamma-aminobutyric acid neurons, which degenerate in Huntington's chorea. The loss of benzodiazepine receptors might explain why the ameliorative effects of benzodiazepines in the early stages of the disease are not sustained in the later stages. 21 references. (Author abstract modified)

002793 Nijeholt, J. Lycklama A.; Korf, Jakob. Dept. of Neurology, Hospital Ziekenzorg, De Ruyterlaan 5, Enschede, The Netherlands **Wilson's disease and monoamines.** Archives of Neurology. 35(9):617-618, 1978.

In a letter to the editor, a study to determine whether changes in central neuronal functioning in Wilson's disease may result in abnormalities in the metabolism of the neurotransmitters, dopamine, and serotonin is reported. The levels of 5-hydroxyindole acetic acid (5-HIAA) and homovanillic acid (HVA) in the lumbar cerebrospinal fluid (CSF) of a 21-year-old man with Wilson's disease were measured before and during treatment with penicillamine. In addition, a probenecid test was performed to obtain some information on the rate of central formation of the acidic metabolites. The results are compared to those

from the patient's sister, who had Wilson's disease but without neurological symptoms, and to those of 33 psychiatric patients who had no major neurological sysmptoms and were chosen because their probenecid levels were comparable with those observed in the two patients with Wilson's disease. In the patient with Wilson's disease who had neurological symptoms, the levels of 5-HIAA and HVA were found to be extremely low. After probenecid treatment, these levels were still found After probenecid treatment, these levels were still found to be abnormally low. During treatment with penicillamine, the patient's condition was greatly improved, and there was a slight increase of the CSF levels of HVA and 5-HIAA. Since HVA in lumbar CSF orignates, at least in part, in the basal ganglia, it is concluded that these fingings point to a direct deficiency in this brain area in Wilson's disease. Since treatment with penicillamine has only minor effects on the low CSF levels of HVA and 5-HIAA, it seems that the damage of central dopaminergic and serotonergic neurons is only partially reversible. 10 references.

002794 no author. no address **Placebos may kill pain by triggering endorphin release.** Medical World News. 19(19):16-17, 1978.

The delivery of a paper by Dr. Jon D. Levine on pain relief from placebos and the response by participants at the Second World Congress on Pain are reported. In Dr. Levine's study, patients suffering from pain due to the extraction of impacted wisdom teeth were given either the opiate antagonist naloxone (10mg), placebo, or both. Patients given naloxone reported significantly more pain than those given placebo. Patients given placebo before naloxone experienced relief with placebo but increased pain with naloxone, suggesting that naloxone blocks endorphin analgesia. Results suggest that placebo may actually trigger the release of endogenous endorphins by some patients. The comments of critics and supporters of Dr. Levine's conclusions are reported.

002795 Ortmann, R.; Nutto, D.; Jackisch, R. Research Department, Pharmaceutical Division, Ciba-Geigy Ltd., Basel, Switzerland **Phosphorylated derivatives of phloretin inhibit cyclic AMP accumulation in neuronal and glial tumor cells in culture.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 305(3):233-240, 1978.

The potencies of polyphloretin phosphate, di-4-phloretin phosphate and phloretin to inhibit the stimulation of c-AMP accumulation by prostaglandins, isoproterenol, and adenosine were studied in 2 clonal cell lines of CNS origin. The sequency of potency to inhibit prostaglandin El(PGEl) effects was the same in neuroblastoma (N4TG3) and human astrocytoma cells (1321N1). The inhibition of PGEl stimulated c-AMP accumulation by the most prostaglandin specific inhibotor, di-4-phloretin phosphate, was rapidly established after its addition, fully reversible after a 30 min preincubation period, and independent of the presence of calcium. A different type of inhibition of PGEl E1 effects by di-4-phloretin phosphate in 1321N1 and N4TG3 cells is suggested. 33 references. (Author abstract modified)

002796 Rappelli, A.; Glorioso, N.: Tedde, R.; Dessi'-Fulgheri, P.; Monaco, F. Cattedra di Patologia Medica II, University of Sassari, Viale S. Pietro, I-07100 Sassari, Italy **Effects of levodopa alone and in combination with dopa-decarboxylase inhibitors on plasma renin activity in patients with Parkinson's disease.** Journal of Neurology, Neurosurgery, and Psychiatry (London). 41(10):915-918, 1978.

The effects of levodopa alone and in combination with dopa-decarboxylase inhibitors on plasma renin activity (PRA) in patients with Parkinson's disease were investigated. PRA of 20 patients with Parkinson's disease was measured in recumbency, upright position, and after frusemide administration. Results show that the renin responses to both stimuli are significantly reduced as compared with those obtained in a group of normal Ss, while recumbent PRA levels of Parkinsonism patients are not significantly lower than those found in recumbent normal Ss. Levodopa treatment, alone or in combination with two different dopa-decarboxylase inhibitors, benserazide and carbidopa, does not modify the renin response to posture or to frusemide. It is concluded that the greater incidence of orthostatis hypotension in patients treated with levodopa seems to be unrelated to any effect of this drug on the renin release. 8 references. (Author abstract modified)

002797 Redmond, Geoffrey P.; Bell, Jennifer J.; Perel, James M. Department of Pharmacology, University of Vermont College of Medicine, Burlington, VT 05401 **Effect of human growth hormone on amobarbital metabolism in children.** Clinical Pharmacology and Therapeutics. 24(2):213-218, 1978.

To determine the effect of human growth hormone (hGH) on human drug metabolism, six hGH deficient children were given single oral doses of amobarbital before and 6 weeks after beginning hGH replacement therapy. Amobarbital was selected as a marker of hepatic microsomal oxidation. Half lives rose from 13.89 plus or minus 2.78 hr to 22.75 plus or minus 3.97 hr, volume of distribution was unchanged, and clearance fell from 62.2plus or minus 15.2ml/kg/hr to 31.2plus or minus 11.4ml/kg/hr. Results indicate that hGH slows the metabolism of amobarbital, probably through an effect on the hepatic microsomal drug oxidizing system. Results are discussed within the context of developmental changes in drug metabolism. 18 references. (Author abstract modified)

002798 Riederer, P.; Youdim, M. B. H.; Birkmayer, W.; Jellinger, K. Ludwig-Boltzmann Institute of Clinical Neurobiology, Lainz Municipal Hospital, Vienna, Austia **Monoamine oxidase activity during (-)-deprenil therapy: human brain post-mortem studies.** Advances in Biochemical Psychopharmacology. 19:377-382, 1978.

Brain monoamine oxidase activity (MAO) was examined postmortem in patients treated with L-DOPA, benserazide, and (-)-deprenil. Results indicate that a daily regimen of (-)-deprenil is sufficient to inhibit brain MAO type B activity by more than 90%, which is in agreement with results obtained previously using platelet MAO as a peripheral marker of CNS MAO. This finding suggests that (-)-deprenil potentiates the antiakinetic effect of L-DOPA in parkinsonian patients by inhibiting brain MAO. 16 references.

002799 Salazar, M.; Sokoloski, T. D.; Patil, P. N. College of Pharmacy, Ohio State University, Columbus, OH 43210 **Binding of dopaminergic drugs by the neuromelanin of the substantia nigra, synthetic melanins and melanin granules.** Federation Proceedings. 37(10):2403-2407, 1978.

At the Annual Fall Meeting of the American Society for Pharmacology and Experimental Therapeutics held in Columbus, August 23, 1977, a paper was presented in which the accumulation of dopaminergic drugs by the human substantia nigra is examined and studies on synthetic melanins and bovine iris melanin granules are discussed for comparison. It was shown that the neuromelanin containing band from the human substantia nigra bound about twice the amount of (3H)chlorpromazine, (3H)haloperidol, and (14C)imipramine as the corresponding nonpigmented band from the superior cerebellar peduncle. The affinity for (3H)chlorpromazine for binding to synthetic L-dopa melanin and bovine melanin granules is the same, but the capacity differs. In both synthetic melanins and melanin granules, a competition between (3H)chlorpromazine and other dopaminergic drugs can be observed. Toxic and beneficial effects of drugs

binding to pigmented cells are considered. 44 references. (Author abstract modified)

002800 Saneto, R. P.; Perez-Polo, J. R.; Werrbach-Perez, K.; Srivastava, S. K. University of Texas Medical Branch, Galveston, TX **Lithium uptake in a human neuroblastoma clonal line.** American Journal of Human Genetics. 30(6):39A, 1978.

A summary of a paper read at the 29th Annual Program of the American Society of Human Genetics, held in Vancouver, Canada, October 1978, is presented. Lithium uptake in cultured human neuroblastoma cells was studied. It was demonstrated that lithium uptake was significantly inhibited by ouabain but not by phloretin in Na-media. Lithium entry in the presence of Na significantly decreased as compared to that of K media. The competitive uptake of Na and lithium in human neuroblastoma cell was not detectable in the red cell. It is suggested that this would indicate that the genetic components of lithium influx in the neuroblastoma cell are expressed differently than that of the red cell. It is concluded that the study of lithium movement components in the red cell may not reflect the components of the neuronal tissue which is the probable site of lithium's therapeutic effect. (Journal abstract modified)

002801 Shimizu, Muneo; Smith, Donald F. Department of Neuropsychiatry, Tokyo Medical College Hospital, 6-7-1 Nishishinjuki, Tokyo, Japan **Relationship between clearance of lithium, potassium and sodium in human mixed saliva.** International Pharmacopsychiatry (Basel). 13(1):34-38, 1978.

The relationship between the clearance of lithium, potassium, and sodium in human mixed saliva was determined directly after a test dose of lithium carbonate (72.9mEq) in two healthy Ss. Lithium clearance in saliva was strongly related to salivary potassium clearance but not to salivary sodium clearance. Stimulation of adrenocortical activity by changing from the recumbent to the upright posture caused salivary sodium clearance to fall, but failed to affect the clearance of lithium and potassium in saliva. The findings show that the secretion of lithium in saliva resembles potassium secretion more than sodium secretion. 8 references. (Author abstract modified)

002802 Sitaram, N.; Moore, Angela M.; Gillin, J. Christian. Building 10, Room 3N224, National Institutes of Health, Bethesda, MD 20014 **Induction and resetting of REM sleep rhythm in normal man by arecholine: blockade by scopolamine. (Unpublished paper).** Bethesda, MD, NIMH, 1978. 15 p.

Arecholine, a cholinergic muscarinic agonist, was administered intravenously 35 min after sleep onset in eight normal volunteers who had been pretreated with either methscopolamine or scopolamine, muscarinic receptor blockers which do not and do cross the blood-brain barrier, respectively. Following methscopolamine, arecholine shortened the REM latency and increased the number of REM periods without altering the duration of individual REM periods or altering the REM to REM intervals. Pretreatment with scopolamine blocked the effects of arecholine. Results support the hypothesis that cholinergic muscarinic mechanisms are involved in the timing but not the duration of REM sleep. 15 references. (Author abstract)

002803 Stillman, Richard C.; Wyatt, Richard Jed; Murphy, Dennis L.; Rauscher, Frederick P. Lab. of Clinical Psychopharmacology, Div. of Special Mental Health Research, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Low platelet monoamine oxidase activity and chronic marijuana use.** Life Sciences (Oxford). 23(15):1577-1581, 1978.

Mean platelet monoamine oxidase (MAO) activity in 26 male marihuana smokers was significantly lower than that in a comparable group of males who did not smoke marihuana. The level of current marihuana use reported by the subjects was significantly and inversely correlated with MAO activity. No acute reduction in MAO activity was found in response to smoking a marijuana cigarette containing 15mg delta-9-tetrahydrocannabinol (THC). Significant in vitro inhibition of MAO activity by THC was detected only at THC concentrations above 0.00001M, which is approximately 100 times the peak plasma concentration seen in vivo following smoking. 17 references. (Author abstract modified)

002804 Tolis, G.; Dent, R.; Guyda, H. Dept. of Medicine, McGill University, Royal Victoria Hospital, Montreal, Quebec, Canada **Opiates, prolactin, and the dopamine receptor.** Journal of Clinical Endocrinology & Metabolism. 47(1):200-203, 1978.

The modulatory effect of dopaminomimetic and antiserotonenergic medication on the hyperprolactinemic effect of tranquilizers and opiates was studied in 10 patients on long-term methadone maintenance for the treatment of heroin addiction. The administration of a dopamine antagonist, chlorpromazine, and two opiates, morphine and methadone, resulted in a significant rise in serum prolactin within 90-150 minutes. Prior administration of dopamine receptor agonists (apomorphine, levodopa, and bromocriptine) blocked this effect. In contrast, cyproheptadine, a serotonin antagonist, did not. It is suggested that the opiates induce hyperprolectinemia in man via dopamine receptor blockade. 19 references. (Author abstract modified)

002805 Whitfield, L. R.; Kaul, P. N.; Clark, M. L. Div. of Clinical Pharmacology, School of Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK 73104 **Chlorpromazine metabolism. IX. Pharmacokinetics of chlorpromazine following oral administration in man.** Journal of Pharmacokinetics and Biopharmaceutics. 6(3):187-196, 1978.

At the 23rd National Meeting of the APhA Academy of Pharmaceutical Sciences, November, 1977, a paper was presented in which data on the apparent absorption and elimination kinetics of orally administered chlorpromazine (CPZ) and its urinary excretion in healthy volunteers was presented. A single oral dose (120mg/m2) of CPZ hydrochloride was administed to four healthy subjects and the blood levels of CPZ were determined with time. Appropriate equations decribing the two compartment open model with zero order absorption and the two compartment model with first order absorption, both with a lag time, were fitted to the observed data using weighted nonlinear least-squares regression analysis. Fitting the two-compartment model with zero order absorption and a lag time to the observed data resulted in a significant reduction of the weighted sum of squared deviations, that is, better correlation between the observed and calculated data, and a closer random scatter of the observed concentration data around the calculated curve with no apparent systematic deviations from the curve. These results suggest that CPZ absorption is zero order. CPZ began to appear in the systemic circulation after a mean lag time of 0.4hours, and continued to be absorbed for approximately 2.9hours. The mean half-lives of the distribution and elimination phases were 1.63 hours and 17.7hours, respectively. 22 references. (Author abstract modified)

002806 Wolpaw, J. R.; Penry, J. K. Epilepsy Branch, Neurological Disorders Program, NINCOS, National Institutes of Health, Bethesda, MD 20014 **Effects of ethanol, caffeine, and placebo on the auditory evoked response.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 44(5):568-574, 1978.

The acute effects of ethanol, caffeine, and placebo on the absolute latencies and amplitudes and on the interhemispheric latency and amplitude differences of two components of the 75-

250msec portion of the human auditory evoked response (AER) to click stimulation were studied. One component is N1P2, the vertex response, and the other is the T-complex. N1P2 is a product of large areas of cortex, and the T-complex is believed to be a product of secondary auditory cortex. Thirty-one normal adults received 3oz of ethanol, 300mg of caffeine, or placebo. Monaural AERs were recorded before intake in all cases, 1 and 4 hours after ethanol and 80 minutes after caffeine or placebo. Blood levels of ethanol and caffeine were measured. Placebo produced mild (20%) decreases in N1P2 amplitude; cafeine did not decrease N1P2 amplitude, but did produce a statistically significant decrease in the latency of the 95msec positive peak (Ta) in the T-complex. Ethanol reduced N1P2 amplitude markedly at 1 hour and mildly at 4 hours. Placebo did not affect hemispheric differences. Caffeine significantly increased the Ta peak ipsilateral vs. contralateral latency difference in three of seven individuals. Ethanol significantly increased it in three of six Ss at 1 hour and in seven of ten at 4 hours, primarily by increasing ipsilateral latencies. 16 references. (Author abstract modified)

002807 Yaksh, Tony L.; Rudy, Thomas A. Department of Neurological Surgery, Mayo Foundation, Rochester, MN 55901 **Narcotic analgetics: CNS sites and mechanisms of action as revealed by intracerebral injection techniques.** Pain (Amsterdam). 4(4):299-359, 1978.

In a study of narcotic analgesics, known regions within the central nervous system are identified where the local application of narcotic agonists can elicit a behaviorally defined elevation of the nociceptive threshold. The pharmacological, anatomical, and behavioral characteristics of these drug/side-effect entities are discussed. Other sites where injections of narcotics have been observed to evoke not analgesia, but some presumed correlate of analgesia are similarly identified and discussed. Where sufficient data are available, an attempt is made to synthesize plausible constructs to explain how narcotics might produce an analgesic effect by an action limited to specific loci. Although the proposed mechanisms are complex, all of the constructs suggest that the analgesic effect of locally applied narcotics may be a consequence of 1) direct passive blockade of nociceptive throughput (spinal cord, lateral mesencephalic reticular formation, nevroreticulo gigantocellularis), and/or 2) a direct or indirect (via efferent projections from the structure injected to other structures) recruitment of active inhibition of nociceptive throughput (mesencephalic central gray). Considerable emphasis is placed upon the latter process. It is concluded that the phenomenon of analgesia produced by the systemic administration of a narcotic depends upon both passive and active processes and that narcotic action in both spinal and supraspinal structures contributes to the manifestations of this behaviorally defined phenomenon. 298 references.

002808 Yamamura, H. I.; Wastek, G. J.; Johnson, P. C.; Stern, L. Z. Dept. of Pharmacology, College of Medicine, University of Arizona Health Sciences Center, Tucson, AZ 85724 **Biochemical characterization of muscarinic cholinergic receptors in Huntington's disease.** In: Jenden, D., Cholinergic mechanisms and psychopharmacology. New York, Plenum, 1978. 885 p. Vol. 24. (p. 35-47).

At the third Symposium on Cholinergic Mechanisms and Psychopharmacology, held in La Jolla, CA, March 1977, a paper was presented on the biochemical characterization of muscarinic cholinergic receptors in Huntington's disease (HD). Three regions of human brain tissue (caudate nucleus, cerebral cortex, and hippocampus) were obtained postmortem from five patients with HD ages 44 to 57 and seven control subjects, ages 32 to 80. The brain tissues were incubated with a high affinity ligand quinuclidinyl benzilate (QNB), and the kinetics of muscarinic cholinerginic receptor binding were assessed. Results indicate that a large number of muscarinic agonists and antagonists effectively inhibited QNB binding. In general, antagonists were 1000 fold more potent as inhibitors than agonists. Equilibrium measurements indicate that QNB associates with the muscarinic receptor at the same rate in all three regions. The displacement of specific 3H-QNB binding by muscarinic agonists and antagonists at relatively low concentrations, while the nicotinic and noncholinergic drugs showed relatively little affinity even at higher concentrations, suggests that QNB is interacting with muscarinic receptors in the human brain. Satchard analysis of kinetic data from the three brain regions at three different tissue concentrations revealed nonsignificant differences for the KD values. Findings suggest that, although the density of muscarinic receptors is decreased in the choreic neostriatum, the remaining receptors have a normal affinity for the ligand. 21 references.

14 MECHANISM OF ACTION: BEHAVIORAL

002809 American Medical Association Council on Scientific Affairs. Council on Scientific Affairs, American Medical Association, 535 North Dearborn Street, Chicago, IL 60610 **Clinical aspects of amphetamine abuse.** Journal of the American Medical Association. 240(21):2317-2319, 1978.

The pharmacological effects of amphetamines, the medical use of amphetamines, and their misuse and abuse are discussed. The diagnosis and treatment of amphetamine abuse, the emergency treatment of amphetamine overdose, and the need for aftercare and rehabilitation of the drug abuser are outlined. Amphetamines and amphetamine-like drugs and prescribed most often to: 1) facilitate weight loss, 2) control behavior disorders of children associated with hyperkinesis and minimal brain dysfunction, and 3) control the symptoms of narcolepsy. Frequently persons who misuse amphetamines do so to try to facilitate performance. Amphetamine abuse can cause three kinds of problems: 1) medical complications such as exacerbation of hypertension and development of arrhythmias or septicemia and endocarditis from unclean needles; 2) emergency conditions such as hyperthermia and convulsions; and 3) signs and symptoms during periods of abstinence that are indicative of drug dependence. It is noted that even without specific therapy, the psychiatric manifestations of amphetamine psychosis usually abate within 6 days after discontinuation of stimulant use. Nonproprietary names and trademarks of drugs are listed.

002810 Barcia, D.; Martinez Pardo, F.; Fuster, P.; Belinchon, L. Departamento de Psiquiatria Facultad de Medicina, Universidad de Murcia, Murcia, Spain **/Preferential indications of depamide according to our experience./** Indicaciones preferentes del depamide segun nuestra experiencia. Actas Luso-Espanolas de Neurologia, Psiquiatria y Ciencias Afines (Madrid). 6(3):249-258, 1978.

The beneficial and detrimental actions of the drug depamide (amide of dipropilacetic) are discussed based on clinical findings. In comparison with psycholeptics that diminish curiosity, spontaneous motility and conditioned reflexes, and with the psychoanaleptics, that increase that conduct, pipropilacetamide does not modify any of the above actions. Dipropilacetamide increases the cognitive capacities, reduces reaction times, improves vigilance, desyncronizes the EEG and does not produce disagreeable sensations. In clinical studies depamide reduces much of the psychotic symptomology. Depamide also increases the potentiality of other drugs, in the sense that the same therapeutic effects can be seen with a smaller dose. To exemplify the findings of the study, case studies are presented, in which the patients fufer from various problems: hysteroepileptic dystimia, cycloid psychosis, and epileptic psychosis. 6 references.

002811 Buchsbaum, M. S.; Davis, G. C.; Bunney, W. E., Jr. National Institute of Mental Health, 5600 Fishers Lane, Rockville, MD 20857 **Effects of naloxone in normal volunteers on somatosensory evoked potentials and pain perception.** Psychophysiology. 15(3):298, 1978.

A summary is presented of a report on somatosensory evoked potentials (EPs) and subjective judgments of electric shock pain intensity which were used to assess modification in pain perception in normal volunteers (10 male, 11 female) given naloxone (2mg), which was delivered to the Seventeenth Annual Meeting of the Society for Psychophysiological Research, held in Philadelphia, October 1977. In the group as a whole, naloxone significantly decreased the latency of the P100 and N140 components, consistent with the postulated antianalgesia. Pain insensitive subjects found shocks more painful on naloxone whereas the sensitive subjects found them less painful. Evoked potentials showed similar group differences. These bidirectional results suggest that individual differences in pain sensitivity may be related to differences in an endorphin system. A modulatory role for endorphins rather than a strictly analgesic one is proposed. (Author abstract modified)

002812 Chapman, C. Richard; Butler, Stephen H. Dept. of Anesthesiology, BB 1415 HSB RN-10, University of Washington, Seattle, WA 98195 **Effects of doxepin on perception of laboratory-induced pain in man.** Pain (Amsterdam). 5(3):253-262, 1978.

A laboratory investigation of pain perception was employed to test the hypothesis that doxepin, a tricyclic depressant, has analgesic properties. Healthy, normal volunteers were tested over a 4 week period during which they repeatedly performed Sensory Decision Theory tasks while undergoing painful dental stimulation. Doxepin and a placebo were administered after baseline measurement for 4 weeks under double-blind conditions. No significant changes due to drug administration were observed in detection threshold or sensory sensitivity indices, but response bias against reporting the stimuli as painful changed dramatically after subjects began ingesting capsules. This effect was evident in both drug and placebo groups, and it was maintained across repeated weeks of testing. It is suggested that the instructions given patients when the drug is administered have a profound effect on pain report. 20 references. (Author abstract modified)

002813 Coates, Thomas J.; Thoresen, Carl E. Center for Educational Research, Stanford University, Stanford, CA 94305 **What to use instead of sleeping pills.** Journal of the American Medical Association. 240(21):2311-2312, 1978.

Insomnia, a complaint denoting varied experiences of poor sleep combined with daytime fatigue, is examined; the effects of hypnotics on rapid eye movement (REM) sleep are discussed; and alternatives to sleeping pills are considered. Procedures such as progressive relaxation, self-hypnosis, autogenic training, meditation, and biofeedback can help patients who are unable to relax physically and mentally at bedtime. But the patient and physician must be aware that it takes time and effort to master these relaxation skills. The patients' lifestyle may be incompatible with good sleep. Patients may have to revise their daytime schedules so that they will be able to relax at bedtime. Those patients whose disturbed sleep stems from family or personal problems (such as chronic depression) may require intensive counseling or psychotherapy. It is suggested that physicians might consider developing collaborative working relatinships with mental health professionals who are competent in providing a variety of services, especially counselors with experience in teaching self-change skills. 12 references.

002814 Cocchi, R.; Ghiglione Rocca, R.; Mastruzzo, A. Ospedale Neuropsichiatrico della Provincia di Cuneo, Racconigi, Italy **/L-glutamine in addition to the usual therapies used for psychiatric patients: a double-blind cross-over trial./** L-glutammina in aggiunta alle usuali terapie in pazienti psichiatrici: saggio a doppio cieco incrociato. Rassegna di Studi Psichiatrici (Siena). 67(2):292-300, 1978.

The effects of L-glutamine on long-term psychiatric patients were studied. In an experimental double-blind cross-over trial, L-glutamine (250mg) and a placebo were added to the usual psychotropic medication of 23 female inpatients. Parameters regarding memory and language were investigated by means of the Digit Span subtest of the Wechsler Adult Intelligence Scale, Thurstone's verbal fluency test, and a verbal disinhibition test. It was found that verbal fluency alone is positively and significantly influenced by the addition of L-glutamine. However, the use of quite restricted experimental parameters could be the cause of fairly limited results. 11 references. (Journal abstract modified)

002815 Domzal, Teofan. Klinika Neurologiczna Centrum Ksztalcenia Podyplomowego WAM, ul. Szaserow 128, 00-909 Warsaw, Poland **/Cholinergic treatment in hyperkineses./** Cholinergizujace leczenie w hiperkinezach. Neurologia i Neurochirurgia Polska (Warszawa). 12/28(3):257-261, 1978.

In a paper presented at the 10th Polish Neurological Society Congress held in Bialystok in 1977, cholinergic treatment in hyperkineses is described. A trial of substitutive treatment was undertaken activating the cholinergic system with a precursor of acetylcholine (dimethyl-amino-ethanol-deanol) with simultaneous inhibition of cholinesterase with prostigmin, using 11 patients with Huntington's chorea, four patients with faciolingual dyskinesis, three patients with torticollis spasmodicus, three patients with maladie des tics, and eight with dyskinesia following previous treatment with L-dopa. Results were compared with previous antidopaminergic treatment (Haloperidol) and with the effects of L-dopa. Differences in the results of cholinergizing and antidopaminergic treatment may indicate nonhomogenous patholigical mechanisms of these hyperkineses. 11 references. (Journal abstract modified)

002816 Ehrhardt, Anke A. New York State Psychiatric Institute, 722 W. 168th St., New York, NY 10032 **Behavioral effects of estrogen in the human female.** Pediatrics. 62(6):1166-1170, 1978.

In a paper presented at the Conference on Estrogen Treatment of the Young, held in Santa Ynez, California, December, 1977, the behavioral effects of estrogen in the human female are reviewed. The role of estrogen in brain differentiation is discussed. Prenatal steroidal effects on human female behavior are covered. The question of timing of estrogen treatment in patients with Turner's syndrome to induce puberty remains controversial; difficulties associated with allowing patients to make these dicisions are observed. Estrogen effects on the behavior of women during menstruation, while taking oral contraceptives, and during menopause are reported. 14 references.

002817 Faber, J.; Kvicala, V.; Sagova, V.; Dvorakova, Z., Mikulenkova, E. Katerinska 30, 120 00 Praha 2, Czechoslovakia / **Effect of learning on the activity of administered methionine in the brain./** Vliv uceni na aktivitu podaneho methioninu v mozku. Ceskoslovenska Neurologie a Neurochirurgie (Praha). 41/74(4):254-260, 1978.

Two groups of four children each were administered methionine and differentially treated, one receiving intensive education, the other intentionally neglected, to investigate the effect of learning on administered methionine activity. An increase in delta activity in increased mental activity in children with aver-

age IQs was found, but inertia of the delta band in children with lower IQs is reported. In the course of the week long teaching process, there was a relative increase in the activity of labeled methionine administered to the taught group of children in contrast to the group of untaught children. Radioactivity was IQ independent as regards time, but may have been dependent on hemispheral differences. A more prominent hemispheral difference was found in children who actually spent more time learning and perhaps also in children with relatively higher IQ values. It is suggested that these results may be indicative of increased protein metabolism in the brain in mental stress. 11 references. (Journal abstract modified)

002818 Feinberg, Irwin; Fein, George; Walker, James M.; Price, Leonard J.; Floyd, Thomas C.; March, Jonathan D. San Francisco Veterans Administration Hospital, 4150 Clement St., San Francisco, CA 94121 **Flurazepam effects on sleep EEG.** Archives of General Psychiatry. 36(1):95-102, 1979.

The initial and short-term effects of flurazepam hydrochloride on the sleep patterns of four normal subjects were examined. The drug substantially suppressed both REM and stage 4 sleep. Computer analysis disclosed that delta wave amplitude was greatly reduced by flurazepam. However, low density delta wave activity permitted the number of delta waves and the time they occupied per night to remain at baseline levels. This finding suggests that sedative hypnotics increase total sleep time by slowing the metabolic processes of sleep so that a longer sleep duration is required for the same biological effects. New observations on the induction times of REM and stage 4 effects are also presented. In general, the distortions in sleep EEG produced by flurazepam qualitatively resemble, but are quantitatively greater than, those produced by barbiturates in equivalent hypnotic doses. 35 references. (Author abstract modified)

002819 Flemenbaum, Abraham. Department of Psychiatry, Louisiana State University Medical School, Shreveport, LA 71130 **On the clinical significance of dopamine receptor hypersensitivity: a primer.** World Journal of Psychosynthesis. 10(3):36-39, 1978.

The clinical significance of reports of dopamine receptor hypersensitivity is examined. The reported findings include increasing effects on some aspects of behavior of the repetitive administration of amphetamine or cocaine. This progressive hypersensitivity appears in the stereotypical behavior of animals and the dopamine linked behavioral phenomena in humans. These findings suggest avenues for research into the pathophysiology of schizophrenia. It is concluded, however, that dopamine receptor hypersensitivity does not provide an adequate explanation for the behavioral phenomena observed, and that factors other than dopaminergic factors must be evaluated. 34 references.

002820 Frowein, H. W.; Sanders, A. F. Institute for Perception TNO, Soesterberg, The Netherlands **Effects of amphetamine and barbiturate in a serial reaction task under paced and self-paced conditions.** Acta Psychologica (Amsterdam). 42(4):263-276, 1978.

The effects of drug conditions (barbiturate, amphetamine, placebo) were investigated in a serial choice reaction time (RT) task under three pacing conditions: self-paced, paced fast (approximately three signals/sec) and paced slow (approximately one signal/sec). Analysis of variance results indicate that drugs affected the RT but not the error scores. Amphetamine was found to speed up the RT while barbiturates slowed it down. It was postulated that barbiturates counteract the arousing effect of time pressure, whereas amphetamine speeds up reaction when the task is not arousing. 17 references. (Author abstract modified)

002821 Gracely, Richard H.; McGrath, Patricia; Dubner, Ronald. Neurobiology and Anesthesiology Branch, National Institute of Dental Research, National Institutes of Health, Bethesda, MD 20014 **Validity and sensitivity of ratio scales of sensory and affective verbal pain descriptors: manipulation of affect by diazepam.** Pain (Amsterdam). 5(1):19-29, 1978.

The results of two experiments suggesting that sensory and affective verbal descriptors provide a valid scaling method which discriminates between the sensory intensity and the affect, or unpleasantness, of electrocutaneous stimuli, are described, and the effects of diazepam on affective descriptor and sensory descriptor responses are discussed. Comparison of verbal descriptor methods and psychophysical methods suggests that only the descriptor method distinguishes between sensory intensity and affect. Diazepam significantly lowered affective descriptor responses without altering sensory descriptor and sensory and affective handgrip responses. It is concluded that sensory and affective verbal pain descriptors may be used as a valid and sensitive tool for the evaluation of pain and pain control methods. 27 references. (Author abstract modified)

002822 Gyselynck-Mambourg, A.-M.; Ylieff, M.; Delwaide, P.-J. Centre Psychogeriatrique ""Le Peri", Montagne Sainte Walburge 4 bis, B-4000 Liege, Belgium /**Revalidation in psychogeriatrics: medical treatment and behavioral methods.**/ Revalidation en psychogeriatrie: traitement medicamenteux et methodes comportementales. Revue de Geriatrie (Paris). 3(2):100-104, 1978.

The clinical effects of piracetam and the effects of behavioral modification on geriatric patients' diurnal incontinence and dressing were studied. In a double-blind experiment conducted for 6 weeks, 29 subjects were given 800mg of piracetam, a medication which acts on the cortex, three times a day. Based on various behavior traits, such as dressing, undressing, spatial orientation, etc.,it was found that piracetam reduces apathy and favorably reorients patients' behavior. In the behavioral modification experiment, an attempt was made to improve the urinary habits of one group and the dressing habits of another group. The first group was urged to relieve themselves at specified times in the beginning, but were gradually given more and more autonomy. The second group began their relearning under controlled conditions (few distractions) and then were encouraged to transfer this knowledge to normal circumstances. Results in both cases were good: 100% of ambulatory and 38% of non-ambulatory patients in the first group showed improvement; and 54% of those in the second group improved. 5 references.

002823 Hrbek, Jan; Komenda, S.; Macakova, J. Dept. of Pathological Physiology, Medical Faculty of the Palacky University, Dr. S. Allende St. 3, 775 15 Olomouc, Czechoslovakia **Effect of meclophenoxate (Cetrexin, Spofa) on the establishment of verbal associations.** Activitas Nervosa Superior (Praha). 20(2):117-118, 1978.

In a paper presented at the 14th Interdisciplinary Conference on the Experimental and Clinical Study of Higher Nervous Functions held at Marianske Lazne, Czechoslovakia, in October 1977, an experiment examining the effect of meclophenoxate (Cetrexin, Spofa) on the establishment of verbal associations in 16 subjects is reported. The investigation sets consisted of two optic, two complex tactile, and two acoustic associations. Between 1 and 2 weeks after the administration of meclophenoxate, an improvement in the number of necessary repetitions and the number of correct responses was observed. It is concluded that the finding was due to a marked improvement in the establishment of artificial conditioned speech connections by means of the complex tactile stimuli. 1 reference.

002824 James, I. M.; Pearson, R. M.; Griffith, D. N. W.; Newbury, Patricia; Taylor, S. H. Taylor: Dept. of Medical Cardiology, General Infirmary, Leeds, England **Reducing the somatic manifestations of anxiety by beta-blockade -- a study of stage fright.** Journal of Psychosomatic Research (Oxford). 22(4):327-337, 1978.

A paper read at the 21st Annual Conference of the Society for Psychosomatic Research, held in London, November 1977, is presented. The effects of oxprenolol taken 90 minutes before the musical performance of 24 string musicians were tested under concert conditions by a double-blind randomized comparison against placebo. The drug attenuated the adverse somatic effects of mental stress on the first musical performance, but there was no significant difference between drug and placebo on the second occasion. It is suggested that intermittent use of small doses of beta-blocking drugs has advantages over the use of tranquilizers or alcohol in allaying the physical results of anxiety. 11 references. (Author abstract modified)

002825 Kahn, Carol. no address **The happiness hormone.** Family Health. 10(12):48-51, 1978.

Beta-endorphin, a bodily substance that reduces pain and tension, produces euphoria and is effective in the treatment of drug addiction is discussed. After tests in which they were given the substance, a hormone that effects happiness, morphine addicts in Taipei and methadone abusers in Los Angeles stopped wanting narcotics. Beta-endorphin may also be useful in treating mental illness. It is concluded that while its high current cost may prevent widespread research, that same high cost will also prevent widespread abuse.

002826 Karhunen, P.; Seppala, T.; Linnoila, M. Dept. of Pharmacology, University of Helsinki, Helsinki, Finland **Counteraction by doxapram of the alcohol-induced impairment of psychomotor skills in man.** Acta Pharmacologica et Toxicologica (Kobenhavn). 43(1):75-77, 1978.

The counteraction by doxapram of the alcohol-induced impairment of psychomotor skills was investigated in six human Ss in a double-blind crossover study. Psychomotor tests were administered 15 min before injection of doxapram hydrochloride or placebo, as well as 2, 30, 60, and 90 min postinjection. Tests included choice reaction test, coordination test (driven at fixed speed), critical flicker fusion test and the measurement of lateral gaze nystagmus. Results suggest that doxapram counteracts some effects of alcohol on psychomotor skills. 5 references.

002827 Kline, Nathan S.; Lehmann, Heinz E. Rockland Research Institute, Rockland State Hospital, Organgeburg, NY 10962 **Clinical observation with beta-endorphin injections.** Psychopharmacology Bulletin. 14(3):12-13, 1978.

Clinical observations of patients administered beta-endorphin injections are presented. The following findings were observed: 1) 1 to 10 mg of beta-endorphin may be safely injected intravenously and will produce distinct psychotropic effects in most individuals; 2) at least three phases of psychotropic actions which differ in quality and in time of occurence may be observed, including a disinhibiting, inhibitory, and a therapeutic effect; 3) naloxone occasionally terminated the inhibitory action of beta-endorphin, but did not interrupt the first or second phase; and 4) certain paresthesias and autonomic effects occurred within seconds after starting the injections in most patients and lasted for a few minutes, although there were no serious immediate or delayed side-effects. 6 references.

002828 Kondo, Kiyotaro; Kabasawa, Takeo. Dept. of Neurology, Brain Research Institute, Niigata University, Asahimachi 1, Niigata, Japan **Improvement in Gilles de la Tourette syndrome after corticosteroid therapy.** Annals of Neurology. 4(4):387, 1978.

A rare postinfectious case of Gilles de la Tourette syndrome, or generalized tic disease, is described. An apparently normal 11-year-old boy developed uncontrollable fits of tendon jerks and brief birdlike cries after an unexplained high fever that subsided spontaneously. The results of electroencephalogram, blood sedimentation, antistreptolysin O titers, C-reactive protein, rheumatoid arthritis, and other laboratory tests are given. Treatment with, in consecutive order, diazepam, carbamazepine, haloperidol, and prednisolone are described. It is suggested by this case history that corticosteroids may be useful in patients in whom there is evidence that Gilles de la Tourette syndrome follows an acute infection. 1 reference.

002829 Kuda, Kenji; Fujitani, Yoshiko; Oikawa, Toshihiko. Dept. of Neuropsychiatry, Tottori University, School of Medicine, Yonago, Japan **Further studies of effects of chlorpromazine on the contingent negative variation.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 32(4):579-584, 1978.

The effect of chlorpromazine (CPZ, 25mg) on contingent negative variation (CNV) at Cz and Oz was studied in nine normal adult males. Two kinds of warning stimulus (S1) and motor response were used. A click as S1 was common to both; while either flashes or electrical stimulation was used as S2. CNV amplitudes after administration of CPZ were decreased significantly at both Cz and Oz when S2 was flashes, and only at Cz when S2 was electrical stimulation. Significant positive correlations of CNV amplitudes between Cz and Oz were found both before and after drug administration. Reaction time to S2 was not affected by CPZ; however, reaction time to flashes was significantly shorter than reaction time to electrical stimulation regardless of preadministration or postadministration of CPZ. 14 references. (Author abstract modified)

002830 Lange, Ehrig; Rossner, Mahnolf; Konig, Liesbeth; Friedemann, Ficker. Neurologisch-Psychiatrische Klinik der Medizinischen Akademie ""Carl Gustav Carus" Dresden, Fetscherstrasse 74, DDR-8019 Dresden, Germany **/Production of clomipramine (monochloroimipramine) in the GDR./** Clomipramin (Monochlorimipramin) in DDR-Produktion. Psychiatrie, Neurologie und Medizinische Psychologie (Leipzig). 30(2):120-122, 1978.

The clinical production and testing of Hydydphene (clomipramine -- AWD) in the GDR is briefly described with reference to previous publications in that area. Results of testing indicate that intravenous clomipramine injections overcome immediate and severe symptoms of depression with an antidepressant action. Clomipramine did not affect the thought patterns and emotions of the patient by interrupting them, as often occurs during electroschock therapy, but rather, the patients were able to be drawn out of their depression in a progressive manner. The use of clomipramine injections is particularly recommended in anxiety psychosis or apathetic depression and severe depression.

002831 Mendelson, Jack H.; Ellingboe, James; Keuhnle, John C.; Mello, Nancy K. Alcohol and Drug Abuse Research Center, Harvard Medical School-McLean Hospital, Belmont, MA **Effects of naltrexone on mood and neuroendocrine function in normal adult males.** Psychoneuroendocrinology (Oxford). 3(3/4):231-236, 1978.

Evidence is presented of a significant increase in integrated plasma luteinizing hormone (LH) levels following oral administration of 50mg of naltrexone to seven healthy adult males who had no past history of opiate use or abuse. All Ss were able to identify naltrexone produced dysphoric effects including fatigue,

sleepiness, light-headedness, nausea, sweating, and occasional feelings of unreality. Three Ss reported recurrent spontaneous penile erections following naltrexone administration. No dysphoric side effects of penile erections occurred following placebo administration. These findings indicate that naltrexone affects both mood states and sexual function in adult males who have no history of opiate abuse and suggest that these effects may be mediated by hypothalamic and pituitary mechanisms which also subserve LH secretory activity. 28 references. (Author abstract)

002832 Meyer-Bahlburg, Heino F. L. New York State Psychiatric Institute, 722 W. 168th St., New York, NY 10032 **Behavioral effects of estrogen treatment in human males.** Pediatrics. 62(6):1171-1177, 1978.

In a paper presented at the Conference on Estrogen Treatment of the Young, held in Santa Ynez, California, December, 1977, the current status of knowledge with respect to prenatal estrogen exposure, estrogen treatment in adolescence and adulthood, and treatment in midlife or later is reviewed. Sex dimorphic behavior, intelligence and general psychopathology are the foci of the discussion. Progesterones and estrogens are discussed together because they are usually administered together. The effects of estrogen treatment for male transsexuals, sex offenders, and in cases of prostate cancer are covered. It is recommended that behavioral changes that may result from estrogen treatment of tall girls be studied. 43 references.

002833 Miller, Loren L.; Cornett, Teresa L. Veterans Administration Hospital, Cooper Drive Division, Lexington, KY 40507 **Marijuana: dose effects on pulse rate, subjective estimates of intoxication, free recall and recognition memory.** Pharmacology Biochemistry and Behavior. 9(5):573-577, 1978.

The effect of marijuana on recognition memory as measured by free recall and signal detection theory, pulse rate and self-ratings of intoxication was evaluated in 16 male volunteers. Marijuana containing 0, 5, 10, or 15mg delta9-tetrahydrocannabinol (delta9-THC) was administered to all Ss by smoking in four sessions separated by a 1 week interval. Free recall was reduced in a dose related manner by the drug, but recognition memory was unaffected. A 2 sec word presentation rate produced inferior recall in comparison to a 4 sec rate, but this variable did not interact with drug condition. Intrusion errors increased following intoxication but this effect was not systematically related to dosage of delta9-THC. Both pulse rate and self-ratings of intoxication increased with dosage. 34 references. (Author abstract modified)

002834 Pentz, Clyde A., III. Syracuse University **The effects of hypertension, antihypertensive medication, and age on specific tasks of the Halstead Neuropsychological Test Battery. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 7813330, HC$15. MF$7.50. 141 p. 1977.

The effects of age, hypertension and antihypertensive medication on performance on the Halstead Neuropsychological Test Battery were determined, along with the appropriateness of medication and plasma renin activity levels in affecting speed, memory, and concept formation components of the battery. Data were obtained from two age groups: 22-36 years and 48-64 years. It was found that: 1) older Ss performed more poorly on a number of subtests, but there were no differences on the Impairment Index; 2) medicated hypertensives had a higher Impairment Index score than the normotensive control group, and they scored lower on several of the subtests; and 3) hypertensives with high plasma renin activity had a lower Impairment Index score than those with normal activity when these scores were adjusted for age. The poorer performance of the medicated hypertensives suggests that antihypertensive medication directly affects performance. The poorer performance of Ss with high plasma renin activity is due to an increased stress placed on the cerebral vessels. The Category Test in the battery allows more subtle discrimination between good and poor performance, while the Impairment Index reveals brain damage only where there is a certainty that it exists. (Journal abstract modified)

002835 Perez, Leon; Marcus-Ofseyer, Braha. Marcus-Ofseyer: George Washington University, Washington, DC 20006 **Case study: the effect of lithium treatment on the behavior and paintings of a psychotic patient with religious and sexual conflicts.** American Journal of Art Therapy. 17(3):85-90, 1978.

The effect of lithium on a chronic schizophrenic as revealed through her art work is reported. Art therapy provided a step by step visual record concerning a patient with whom communication was difficult not only because of her illness but also because of a language barrier. Both the beneficial effect of lithium on her affective disorder -- the patient's mood shifted from intense agitation to relative calm -- and its failure to influence her delusional ideas are strikingly demonstrated. Her inner conflicts about her religious and sexual identity also are revealed in the rich imagery. The experience points to the usefulness of art therapy as a means for studying the effect of lithium treatment on the affective symptoms of schizophrenia and for helping to distinguish between thought disorder and affective disorder. 9 references. (Author abstract modified)

002836 Robinson, Connie Ruth. University of Alabama **A study of the effects of niacin upon sleep and brain monoamines. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 7800632, HC$15. MF$7.50. 157 p. 1976.

The effects of nicotinamide on sleep were investigated. Six normal subjects and two insomniacs who had sleep recordings made of their rapid eye movement (REM) sleep were administered nicotinamide. Groups of mice were also injected with nicotinamide in varying dosages for 14 days after which brain sections were assayed for 5-hydroxy-tryptamine (5-HT), 5-hydroxyindoleacetic acid (5-HIAA), and norepinephrine (NE). Results showed that nicotinamide altered the levels of the neurotransmitters, 5-HT and NE, and the metabolite, 5-HIAA. Correlation coefficients showed that 5-HT changes had greater influence over NE in the telencephalon while 5-HIAA changes most influenced levels of NE in the lower brain sections. In normal human sleepers REM sleep increased significantly during nicotinamide administration; after 3 weeks, insomniacs' awake time decreased remarkably and REM increased significantly. (Journal abstract modified)

002837 Saarinen, A.; Myllyla, V. V.; Tokola, O.; Hokkanen, E. Department of Neurology, University of Oulu, SF-90220 Oulu 22, Finland **Effect of a slow release preparation of levodopa on Parkinson's disease in combination with a peripheral decarboxylase inhibitor.** Acta Neurologica Scandinavica (Kobenhavn). 58(6):340-349, 1978.

Plasma concentrations of levadopa were studied in parkinsonian patients after therapeutic oral levadopa-carbidopa doses, under the hypothesis that the wide fluctuations observed in plasma levodopa levels could be considerably reduced by the addition of a slow release levodopa preparation. This kind of combination medication was given to 15 parkinsonian patients whose earlier therapy had proven inadequate. With the combination medication, levodopa-carbidopa, on an average 420mg/42mg combined with 950mg of levodopa in slow release form, a statistically significant improvement in parkinsonian signs could be achieved without any worsening of the side-effects. The results suggest that parkinsonian patients may tolerate much higher daily levodopa doses if the fluctuations in plasma level of

the drug can be diminished. 8 references. (Author abstract modified)

002838 Saletu, Bernd; Grunberger, Josef. Section of Pharmacopsychiatry, Psychiatrische Universitatsklinik, A-1090 Vienna, Austria **Assessment of psychoactivity and pharmacodynamics of a cerebral vasodilating hexobendine-combination by quantitative electroencephalographic and psychometric analyses.** Progress in Neuro-Psychopharmacology (Oxford). 2(5/6):543-551, 1978.

Encephalotropic, psychotropic and pharmacodynamic properties of orally and intravenously administered Instenon forte and intravenously injected Instenon ampuls were studied in a double-blind placebo controlled trial in 10 normal volunteers. Power spectral analysis of the EEG showed a decrease in delta waves and an increase of alpha and beta waves as compared with placebo. Psychometric tests demonstrate especially after high doses, an increase in psychomotor activity, critical flicker frequency; improvement in quantitative and deterioration in qualitative aspects of attention; and improvement of mood and affectivity. These findings indicate that Instenon forte induces and increases vigilence. The potency and duration of action of the various oral and intravenous preparations are discussed. 26 references. (Author abstract)

002839 Scharbach, H. Centre Hospitalier Regional de Nantes, rue de Gigant 9, F-44000 Nantes, France **/Current information on the use of beta-blocking agents in psychiatry./** Bilan actuel sur les substances beta-bloquantes dans leurs indications psychiatriques. Acta Psychiatrica Belgica (Bruxelles). 78(2):358-373, 1978.

Current information from experiments on the use of beta-blocking agents, particularly in anxicus or depressive anxious patients, is reviewed. The anxiolytic effect is of particular interest, especially in cases of somatic anxiety, where it is superior to the benzodiazepines. Antipsychotic effects have also been noted. In one experiment, low doses of the beta-blocking agents aldeprenolol, pindolol, and oxyprenol were administered to 100 psychiatric patients. Results show a reduction in somatic anxiety and anxiety related problems such as disturbed sleep patterns, reduced attention span, emotivity, and stress. 26 references.

002840 Van Dyke, C.; Jatlow, P.; Ungerer, J.; Barash, P.; Byck, R. Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Cocaine and lidocaine have similar psychological effects after intranasal application.** Life Sciences (Oxford). 24(3):271-274, 1979.

Three matched doses (0.19, 0.38, and 0.75mg/kg) of cocaine and lidocaine were administered intranasally to three male subjects who had previous experience with cocaine self-administration. Psychological ratings were similar for the two drugs at all three doses. Results indicate that the subjects were not able to discriminate between the drugs. 16 references. (Author abstract modified)

002841 Vlasov, N. A. Otdel patologii vegetativnoy nervnoy sistemy I Moskovskogo meditsinskogo instituta im. I. M. Sechenova, Moscow, USSR **/The effect of gamma-aminobutyric acid derivatives on sleep disturbances in neuroses./** Vliyaniye proizvodnykh gamma-aminomaslyanoy kisloty na narusheniya sna pri nevrozakh. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 85(2):174-177, 1978.

Electropolygraphic tests were carried out on 34 mental patients suffering from insomnia of various types, in order to determine the effects of two gamma-aminobutyric acid derivatives on sleep structure. The derivatives were found to cause an increase in total sleep duration due to an accretion of the basic sleep stages and a statistically significant reduction in the number of spontaneous nocturnal awakenings. The data show a tendency toward an increase in the number of second stage sleep spindles, of delta-index in the third and fourth stages, and of the average number of rapid eye movements in the absence of any marked changes in their specific occurrence per time unit. The derivative sodium oxybutyrate was found to have a more pronounced effect than phenibutol. 7 references. (Journal abstract modified)

002842 Weinberg, Avrom Michael. Boston University Graduate School **Personality factors affecting response to antianxiety agents and placebo in a laboratory model of anxiety. (Ph.D. dissertation).** Dissertation Abstracts International. 39(5):2531-B, 1978. Ann Arbor, Univ. Microfilms No. 7819839, 196p., 1978.

To determine whether acquiescence (Acq) and physiological awareness (PA) predict psychophysiological and subjective response to anxiolytic medications and placebo in a laboratory model of anxiety, subjects were placed in a stress situation of public speaking where anxiety was manipulated experimentally. Four hypotheses were tested: 1) high Acq subjects will show less anxiety increase in the stress situation than low Acq subjects on placebo; 2) low Acq subjects will show less anxiety increase in the stress situation than high Acq subjects on active medication; 3) high PA subjects will show less anxiety increases in the stress situation than low PA subjects on placebo; and 4) low PA subjects will show less anxiety increase in the stress situation than high PA subjects active medication. The predictive value of reported level of Public Speaking Phobia (Pho) was evaluated. Results show that none of the formal hypotheses received experimental confirmation. A new theory, developed as an interpretative response to unexpected findings from the data analyses, is systematically presented. The basis of the theory is a personality variable, the Public Image Protection (PIP) factor, and the theory in toto is called PIP Effect Theory. It is theorized that the PIP factor causes intense anxiety to be generated when a low Pho/high PIP subject fears that he has taken a pill which may undermine his capacity to render optimal performance at a public speaking situation. Clinical and experimental implications of the PIP Effect Theory are noted. (Journal abstract modified)

002843 Zaimov, Kosta; Kokoshkarova, Anna. Psychiatrische Universitatsklinik, Boulevard Georgi Sofirski 1, Sofia 31, Bulgaria **/A study of the effects of chlorpromazine and amphetamine upon incidental memory and its relation to the introversive-extraversive structure of the personality./** Untersuchung der Einwirkung von Chlorpromazin und Amphetamin auf die zufallige Merkfahigkeit und ihren Zusammenhang mit dem introversen-extraversen Gefuge der Personlichkeit. Psychiatrie, Neurologie und Medizinische Psychologie (Leipzig). 30(10):593-598, 1978.

The effects of chlorpromazine and amphetamine upon incidental memory and its possible dependence on the introversive or extraversive personality structure were investigated. A total of 54 subjects were divided into control, amphetamine, and chlorpromazine groups. It was found that chlorpromazine tends to lessen the accuracy and extent of incidental memory and increase the instances of inaccurate remembrances. Amphetamine increased the extent and accuracy of incidental memory. Incidental memory was found to be less extensive in introverted personalities than in extraverted personalities. 12 references. (Journal abstract modified)

15 TOXICOLOGY AND SIDE EFFECTS

002844 Angrist, Burton M. New York University Medical School, New York, NY **Toxic manifestations of amphetamine.** Psychiatric Annals. 8(9):13-15, 18, 1978.

Pathologic conditions associated with the ingestion of CNS stimulants, including amphetamine, are reviewed, and appropri-

ate therapy for these reactions is described. People vary enormously in their sensitivity to CNS stimulants, but the following sequence of effects is usually observed: 1) euphoria, 2) anxiety, 3) early psychotic manifestations, 4) frank delusional states, 5) auditory or visual hallucinations, and 6) toxic confusion. Treatment for toxic manifestations of amphetamine include hospitalization, monitoring of vital signs, and treatment with major tranquilizers. The relative merits of chlorpromazine and haloperidol for treating patients with stimulant psychoses are discussed. 12 references.

002845 Beitman, Bernard D. Department of Psychiatry and Behavioral Sciences, Clinic '2, GI-15, University of Washington School of Medicine, Seattle, WA 98195 **Tardive dyskinesia reinduced by lithium carbonate.** American Journal of Psychiatry. 135(10):1229-1230, 1978.

A case report describing the reemergence of tardive dyskinesia (which had been quiescent for several years) due to the administration of lithium carbonate is presented. A 56-year-old woman had suffered from recurrent depressive episodes since 1960 and had been treated with electroconvulsive therapy and tricyclic antidepressants. She was treated with thioridazine for 6 years until dyskinesia developed in 1973. Four years later, the dyskinesia reappeared after more than a year of lithium therapy. Addition of trihexyphenidyl alleviated the symptoms. Possible explanations of neuroleptic-induced tardive dyskinesia are discussed. 7 references.

002846 Brenner, Ira; Rheuban, William J. Department of Psychiatry, University of Virginia Medical Center, P.O. Box 203, Charlottesville, VA 22901 **The catatonic dilemma.** American Journal of Psychiatry. 135(10):1242-1243, 1978.

A case report of the treatment of catatonic schizophrenia and superimposed neuroleptic catatonia is presented. It is noted that catatonia can be a side-effect of a high potency neuroleptic treatment for schizophrenia. Noncatatonic patients who develop this as a complication are prone to pulmonary emboli and other serious side-effects. The patient was a 19-year-old college student who suffered volitional conflicts following hospitalization for symptoms of schizophrenia. Such volitional conflicts are characteristic of catatonic schizophrenia and do not occur in a pure neuroleptic-induced stupor. The development of aspiration pneumonia indicated an additional catatonic condition caused by the medication. 10 references.

002847 Chouinard, Guy; de Montigny, Claude; Annable, Lawrence. Department of Psychiatry, McGill University, Montreal, Quebec, Canada **Tardive dyskinesia and antiparkinsonian medication.** American Journal of Psychiatry. 136(2):228-229, 1979.

The effects of administration and subsequent withdrawal of the central anticholinergic agent procyclidine HCl in extrapyramidal symptoms were examined in 20 schizophrenic patients with significant tardive dyskinesia. Procyclidine had an effect on tardive dyskinesia opposite to that on parkinsonism, improving the latter but exacerbating the dyskinetic movements. Findings are consistent with the dopamine supersensitivity hypothesis of tardive dyskinesia: procyclidine may have exacerbated dyskinetic symptoms by its dopamine reuptake blocking property and/or its central anticholinergic activity. 10 references.

002848 Cohen, Kenneth L.; Cooper, Richard A.; Altshul, Susan. West Haven Veterans Administration Hospital, West Haven, CT 06516 **Prolactin levels in tardive dyskinesia.** New England Journal of Medicine. 300(1):46, 1979.

The prolactin response to stimulation with thyrotropin releasing factor was examined in four schizophrenic patients with tardive dyskinesia. The patients ranged in age from 33 to 64 years, with a mean of 46 years. The response was normal in all four patients, suggesting that prolactin secretion may not reflect central dopaminergic hypersensitivity, or that this hypersensitivity may not exist in tardive dyskinesia. The limitations of the study include the impossibility of withdrawing neuroleptic drugs before testing with thyrotropin releasing factor, and the clinical grounds for the diagnosis of tardive dyskinesia. Studies with larger groups of patients are recommended. 5 references.

002849 Colman, Arthur D. University of California Medical Center, San Francisco, CA 94143 **Possible psychiatric reactions to monosodium glutamate.** New England Journal of Medicine. 299(16):902, 1978.

Two case reports of acute and chronic psychiatric responses to monosodium glutamate are presented, and the possibility that there are a number of persons suffering such reactions to monosodium glutamate who remain unaware of the cause of their disorders is discussed. In addition to the typical acute 5 to 12 hour monosodium glutamate reaction, a longer term psychologic effect characterized by depression, gloomy fantasies, and paranoid perceptions is noted. The second case report is of the 9-year-old son of the first patient. In addition to the acute reaction, the boy had symptoms of bladder and bowel incontinence and intermittent hyperactivity. These symptoms disappeared within 2 weeks of being placed on a diet free of monosodium glutamate. 4 references.

002850 Crome, P.; Braithwaite, R. A. Poisons Unit, Guy's Hospital, London SE1 9RT, England **Relationship between clinical features of tricyclic antidepressant poisoning and plasma concentrations in children.** Archives of Disease in Childhood (London). 53(14):902-905, 1978.

Clinical features and drug plasma concentrations were studied in 13 children admitted to hospital with tricyclic antidepressant poisoning. Patients with plasma concentrations below 500 mcg/l had anticholinergic signs and increased reflexes but did not have convulsions, cardiac arrhythmias, or prolonged coma. The diagnosis of poisoning in two of these cases was made only by toxicological analysis. It is conluded that quantitative estimation of tricyclic antidepressants is useful in atypical or severe poisoning both to reach the diagnosis and to give an idea of the likely duration of symptoms. 12 references. (Author abstract)

002851 Cutler, Neal R.; Heiser, Jon F. Biological Psychiatry Branch, National Institute of Mental Health, Bldg. 10, 3S239, Bethesda, MD 20014 **Recurrent leucopenia following treatment with thiothixene and haloperidol respectively. (Unpublished paper).** Bethesda, MD, NIMH, 1978. 8 p.

A case history of a recurrent leucopenia developing in a patient following treatment with thiothixene and haloperiol is reported. The 27-year-old patient was admitted to a hospital for treatment of lye ingestion following a suicide attempt. The patient developed a severe leucopenic count while being treated with thiothixene and about 3 weeks later developed another leucopenic state while being treated with haloperidol. His leucocyte count rose to normal within a few days after each antipsychotic agent was discontinued. While both immunologic and toxic mechanisms for the drug-induced leucopenias habe been implicated, it was impossible to establish either cause due to the unavailability of both bone marrow and antibody studies. 4 references.

002852 Cuzzolaro, M.; Bordi, M.; Scavo, A.; Zanda, G. Universita degli Studi di Roma, Facolta di Medicina e Chirurgia, I Cattedra di Psichiatria, Rome, Italy /**Considerations concerning a clinical experience with fluphenazine decanoate.**/ Considerazioni intorno a una esperienza clinica con decanoato di flufenazina. Rassegna di Studi Psichiatrici (Siena). 67(2):281-291, 1978.

Observations on the clinical use of the tranquilizer fluphenazine decanoate are presented. Side-effects, associations, and interruptions in the comparative treatments of long-term and short-term psychiatric patients are considered. Several psychological implications connected with the choice and use of the drug are analyzed, and important questions are posed concerning the specific relationship between the type of drug used and the psychological mechanism of overcoming the crisis. (Journal abstract modified)

002853 Donlon, Patrick T.; Hopkin, John; Schaffer, Charles B.; Amsterdam, Ezra. Department of Psychiatry, School of Medicine, University of California, Davis, 3340 V Street, Sacramento, CA 95187 **Cardiovascular safety of rapid treatment with intramuscular haloperidol.** American Journal of Psychiatry. 136(2):233-234, 1979.

The effects of rapid treatment of schizophrenia with intramuscular haloperidol on heartrate and blood pressure were investigated in 25 acutely psychotic patients whose mean age was 25 years. During the 6 hour study period the total dose administered was 22.5mg (range 10mg to 40mg). Analysis of variance indicated that there were no significant reductions in mean values for blood pressure and heartrate: both decreased gradually within the normal range. Only one patient showed a clinically significant decrease in blood pressure, which returned to pretreatment levels approximately 6 hours after initial injection. Results indicate a high degree of cardiovascular safety of intramuscular administration of haloperidol to healthy patients who require moderate treatment doses at 30 min intervals. Risk may be greater in elderly and/or medically ill patients. 6 references.

002854 Dysken, Maurice W.; Merry, William; Davis, John M. Illinois State Psychiatric Institute, 1601 W. Taylor, Chicago, IL 60612 **Anticholinergic psychosis.** Psychiatric Annals. 8(9):30-31, 35,39,42, 1978.

Central and peripheral signs and symptoms of anticholinergic psychosis, reported and potential sources of anticholinergic toxic psychosis, and treatment of anticholinergic psychosis are described. Anticholinergic toxicity may occur in persons who are given preanesthetic medication such as atropine or scopolamine or in patients who are prescribed anticholinergic drugs for Parkinsonism. When certain combinations of drugs with anticholinergic properties are used, an additive effect may also result in a toxic psychosis. An overdose, either with suicidal intent or in pursuit of hallucinogenic and euphoriant effects is another situation which the central anticholinergic syndrome may arise. Although in most cases discontinuation of anticholinergic drugs will be sufficient pharmacologic management, physostigmine can be an important, if not lifesaving, aid in the treatment of this condition. 21 references.

002855 Fauman, Beverly J.; Fauman, Michael A. Dept. of Psychiatry, University of Chicago Hospitals, Chicago, IL 60637 **Phencyclidine Psychosis.** Illinois Medical Journal. 154(4):324-325, 1978.

A previously healthy 39-year-old man with no personal or family history of psychiatric disturbance developed phencyclidine psychosis requiring several weeks hopitalization after smoking marihuana. Results suggest that with the increasing use of phencyclidine, even psychologically healthy people who are not typical drug users may develop a phencyclidine psychosis. 12 references. (Author abstract modified)

002856 Fink, Edward B. 345 Blackstone Blvd., Providence, RI 02906 **Unexpected and prolonged akinesia: a case report.** Journal of Clinical Psychiatry. 39(11):817-818, 1978.

The case of a male college student who experienced akinesia lasting almost 3 weeks following withdrawal from relatively brief, low dose neuroleptic treatment is described. The literature is reviewed and the duration of extrapyramidal side-effects in the case are examined. These syndromes are often undiagnosed or misdiagnosed and lead to unnecessary morbidity and noncompliance with recommended pharmacotherapy. 8 references. (Author abstract)

002857 Gagrat, Dinshah; Hamilton, James; Belmaker, Robert H. Veterans Administration Hospital, Wood (Milwaukee), WI 53193 **Intravenous diazepam in the treatment of neuroleptic-induced acute dystonia and akathisia.** American Journal of Psychiatry. 135(10):1232-1233, 1978.

The effectiveness of intravenous diazepam in alleviating neuroleptic-induced dystonia and akathisia was investigated. Dystonia is characterized by acute spasm of a muscle group, and akathisia is defined as acute restlessness. A total of 40 intravenous treatments were administered to 27 patients in a double-blind design. Subjects were rated for severity of symptoms before treatment and 5, 15, 30, and 120 minutes after treatment. Intravenous diazepam was found to be as effective as treatment with diphenhydramine, a standard anticholinergic. 10 references.

002858 Gelenberg, Alan J.; Doller, Joanne C.; Schooler, Nina R.; Mieske, Marlene; Severe, Joanne; Mandel, Michael R. Massachusetts General Hospital, Boston, MA 02114 **Acute extrapyramidal reactions with fluphenazine hydrochloride and fluphenazine decanoate.** American Journal of Psychiatry. 136(2):217-219, 1979.

In a four center collaborative study, extrapyramidal symptoms (EPS) of fluphenazine hydrochloride and fluphenazine decanoate were compared in 290 schizophrenic inpatients. Results failed to reveal significant differences between the oral and depot fluphenazine in the occurrence of akathisia or Parkinson's syndrome. In addition, no correlations were found between the occurrence of any of the signs of these two disorders and age, sex, race, history of EPS, or previous anti-Parkinsonian drug use. Benztropine use was significantly related to the presence of EPS. Data indicate that, despite their relatively high incidence, akathisia and Parkinsonism are not serious problems during the first 7 weeks of treatment with either fluphenazine. 10 references.

002859 Geller, Barbara; Greydanus, Donald E. Department of Child Psychiatry, New York University Medical Center, 550 First Avenue, New York, NY 10016 **Haloperidol-induced comatose state with hyperthermia and rigidity in adolescence: two case reports with a literature review.** Journal of Clinical Psychiatry. 40(2):102-103, 1979.

Two adolescents (a 15-year-old female and a 12-year-old male) who developed severe extrapyramidal and hypothalamic reactions due to haloperidol therapy are described. Administration of trihexyphenidyl in one case, and apresoline in the second, resulted in alleviation of symptoms. Syndrome malin (neuroleptic malignant syndrome) has been rarely reported as a result of using haloperidol in children and youth. Diagnosis and management of the syndrome are reviewed, and caution is urged in use of haloperidol. 11 references. (Author abstract modified)

002860 Gershon, Elliot S.; Goldstein, Robert E.; Moss, Arthur J.; van Kammen, Daniel P. Biological Psychiatry Branch, National Institute of Mental Health, Bethesda, MD, 20014 **Psychosis with ordinary doses of propranolol. (Unpublished paper).** Bethesda, MD, NIMH, 1978. 6 p.

A case history of a patient who developed paranoid psychosis resembling acute schizophrenia during administration of relatively low doses of propranolol is reported. The patient had no preexisting psychiatric illness. Administration of 80-160mg propranolol daily in divided doese resulted in vivid nightmares and subsequent auditory and visual hallucinations and paranoid delusions. All psychotic manifestations disappeared within 48 hours of discontinuing propranolol. The case demostrates that psychosis can develop in a normal person given propranolol in doses at or below those commonly used to treat many cardiovascular and central nervous disorders. 5 references. (Author abstract modified)

002861 Ghose, Karabi. Ciba-Geigy Research Center, Goregaon (East), Bombay 400 063, India **Effect of carbamazepine in polyuria associated with lithium therapy.** Pharmakopsychiatrie/ Neuro-Psychopharmakologie (Stuttgart). 11(5):241-245, 1978.

Oral carbamazepine (300-600mg/day for 6 weeks) was no more effective than placebo in treating polyuria and polydipsia associated with long-term lithium therapy in 10 patients with affective disorders. Plasma and urine osmolality were within normal range in these patients, and no antidiuretic response to subcutaneous injection of Pitressin was observed. The drop out rate due to severe side-effects (ataxia, dizziness, restlessness, and confusion) was 50%. Results suggest that lithium exacerbates carbamazepine-induced side-effects (or vice versa), possibly through the drugs' mutual effects on sodium metabolism or on nervous conduction velocity. Simultaneous administration of these two drugs should be avoided. 22 references. (Author abstract modified)

002862 Goldfrank, Lewis; Bresnitz, Eddy. Albert Einstein College of Medicine, New York, NY **/Coma resulting from CNS depressants./** The deep sleep. Hospital Physician. 14(7):26-30, 37, 1978.

The treatment of coma from CNS depressants is examined. Five broad categories of these drugs are listed: 1) benzodiazepines; 2) nonbenzodiazepines; 3) propanediol; 4) piperidinediones; and 5) quinazolinones. Brand names and clinical data are given for each. Reed's classification and management techniques for coma are outlined. Effects of chronic sedative hypnotic use are discussed as well as factors predisposing patients to increased sedative hypnotic toxicity. Criterion for dialysis are offered.

002863 Greenland, Philip; Southwick, William H. Department of Medicine, Strong Memorial Hospital, 601 Elmwood Ave., Rochester, NY 14642 **Hyperthermia associated with chlorpromazine and full-sheet restraint.** American Journal of Psychiatry. 135(10):1234-1235, 1978.

A case report of a patient who suffered profound hyperpyrexia while under full sheet restraint and chlorpromazine treatment is presented. An 18-year-old male was admitted to a psychiatric service because of agitation and combative behavior. He suffered two episodes of extremely high fever while under restraint. It is hypothesized that the mechanism of fever was a chlorpromazine-induced abnormality of central thermoregulation combined with an inability to evaporate sweat due to the nylon restraints. 10 references.

002864 Grunhaus, L.; Sancovici, S.; Rimon, R. Hadassah Medical Center, Ein Karem, Jerusalem, Israel **Neuroleptic malignant syndrome due to depot fluphenazine.** Journal of Clinical Psychiatry. 40(2):99-100, 1979.

Diagnostic difficulties which may be encountered in patients treated with depot neuroleptics are illustrated in a case study. At time of admission, a 19-year-old male patient presented with disorientation, psychomotor restlessness, and delusional and hallucinatory thought content. The patient was initially treated with chlorpromazine, haloperidol, and trihexylphenidyl. Fluphenazine treatment was initiated a week after admission. Psychotic symptoms subsided and the patient was discharged after 6 weeks. Medication at this time included 17.5mg fluphenazine intramuscularly every 2 weeks and 10mg trihexylphenidyl per day. Extrapyramidal symptoms developed the day following discharge and continued despite discontinuation of medication. The patient became lethargic and eventually incontinent and comatose. Following exclusing of other possible diagnoses, intensive parenteral antiparkinsonian therapy was initiated and symptomatology progressively resided. 17 references.

002865 Hale, Claire; Heins, Terence. Department of Psychiatry, Queen Elizabeth Hospital, Woodville, S.A. 50011, Australia **Tardive dyskinesia and antihistamines.** Medical Journal of Australia (Glebe). 1(2):112-113, 1978.

A case of tardive dyskinesia due to the prolonged administration of antihistamines is reported. Of two antihistamines used over a number of years, the phenothiazine promethazine is closest in structure to drugs previously implicated as causes of tardive dyskinesia. Haloperidol was successful in suppressing the movements of tardive dyskinesia. The lack of change in the tardive dyskinesia when haloperidol was discontinued over a 10 month followup supports previous reports of the relative irreversibility of this syndrome. 6 references.

002866 Hartley, L.; Henry, T.; Couper-Smartt, J. Dept. of Psychology, University of Leicester, Leicester LE1 7RH, England **Chlorpromazine and serial reaction performance.** British Journal of Psychology (London). 69(2):271-276, 1978.

The effect of 25mg or 75mg of chlorpromazine on the serial reaction performance of 12 male subjects was studied. Speed or number of correct responses was reduced by the high dosage, and errors of commission and omission were increased. Results show that the adverse effect of the drug upon speed appeared only at the end of the half hour test, but the adverse effect upon gaps and errors was apparent throughout the test, and there was no interaction with test duration. 12 references. (Author abstract)

002867 Holmstedt, Bo; Nordgren, Ingrid; Sandoz, Marianne; Sundwall, Anders. Dept. of Toxicology, Swedish Medical Research Council, Karolinska Institutet, S-10401 Stockholm, Sweden **Metrifonate: summary of toxicological and pharmacological inforamtion available.** Archives of Toxicology (Berlin). 41(1):3-29, 1978.

Available toxicological and pharmacological information on metrifonate, an organophosphorus compound, is summarized. The compound was introduced as an insecticide in 1952 and in the treatment of schistosomiasis in 1960. The compound is unique in that it has been claimed not to be a direct acting cholinesterase inhibitor but is transformed nonenzymatically into an active component dichlorvos,2,2-dichlorovinyl dimethyl phosphate (DDVP). The evidence for this transformation has mostly been indirect. Recently it has been proven chemically and quantitatively that this transormation occurs in the animal body (Nordgren et al.,1978). Mentrifonate is the sole organophosphorus compound currently studied clinically in schistosomiasis. It is suggested that further more detailed studies of S. haematobium and S. mansoni are necessary. This should include studies of the enzymic properties of the worms and the reaction of their esterases toward both metrifonate and DDVP as well as the pharmacokinetics of these compounds in man. Additionally, there are still unsolved discrepancies reported regarding organ toxicity of the compound which may be due to different grades

of parity of the test material. 111 references. (Author abstract modified)

002868 Iversen, Bjarne M.; Willassen, Yngvar; Bakke, Olav M. Medical Department A., Laboratory of Clinical Biochemistry, Haukeland Sykehus, Bergen, Norway **Charcoal haemoperfusion in nortriptyline poisoning.** Lancet (London). 1(8060):388-389, 1978.

Treatment of nortriptyline toxicity in a 55-year-old female what attempted suicide by charcoal hemoperfusion is discussed in a letter. Serum nortriptyline concentrations were determined to be 1259mg/l before hemoperfusion and 867mg/l after 3 hr hemoperfusion. Although no clinical improvement was noted during the procedure, the patient regained consciousness on the third day after admission. She admitted having ingested a dose of approximately 1250/mg. Despite the reduction in venous blood concentration, only about 1% of the amount ingested was removed. This apparent discrepancy is probably due to the high degree of tissue binding. It is concluded that while hemoperfusion is moderately effective as judged by the extraction ratio of nortriptyline across the apparatus, it does not remove significant amounts of the drug from the body.

002869 Jaffe, Kenneth; Zisook, Sidney. Dept. of Psychiatry, University of Texas Medical School, PO Box 20708, Houston, TX 77025 **Galactorrhea in a patient treated with amoxapine.** Journal of Clinical Psychiatry. 39(11):821, 1978.

A case of galactorrhea with amoxapine, a new antidepressent chemically distinct from other tricyclic antidepressents, is reported. Galactorrhea is a rarely reported complication of tricyclic antidepressants. The development of galactorrhea in a patient treated with amoxapine suggests the possibility of significant dopamine blocking activity in this drug. 9 references. (Author abstract modified)

002870 Jefferson, James W.; Greist, John H. Center for Health Sciences, University of Wisconsin, Madison, WI 53706 **Lithium intoxication.** Psychiatric Annals. 8(9):47, 50-56, 1978.

The signs, causes, and treatment of lithium intoxication are discussed. Despite the general awareness of the narrow therapeutic ratio of lithium and close attention to its potential hazards, lithium intoxication in patients treated for mania is not rare. Although there is no constellation of symptoms that could be considered characteristic of lithium intoxication, lithium intoxication prodromal symptoms, neurological symptoms of advanced lithium intoxication, and other symptoms of advanced intoxication are described. Causes of lithium intoxication include: errors in dose administration, impaired lithium excretion, sodium imbalance, postpartum physiological changes, predisposition to lithium toxicity, and drug interactions. Once the diagnosis of lithium poisoning has been made, efforts must be directed at minimizing further absorption, maximizing rate of excretion, and providing general support. Measures to minimize the likelihood of lithium poisoning are described. 50 references.

002871 Johnson, M. K. MRC Toxicology Unit, Medical Research Council Laboratories, Woodmansterne Road, Carshalton, Surrey, SM5 4EF, England **The anomalous behaviour of dimethyl phosphates in the biochemical test for delayed neurotoxicity.** Archives of Toxicology (Berlin). 41(1):107-110, 1978.

The delayed neurotoxic effects of dimethyl phosphates was studied with hens. Doses caused high inhibition of brain neurotoxic esterase (NTE) but no ataxia. Less inhibition of NTE was seen in spinal cord than in brain. Di-isopropyl phosphorofluoridate caused equal inhibition of NTE in brain and cord. When dosing with dimethyl phosphates was repeated, NTE inhibition in cord increased and pair dosed birds became ataxic. In vitro brain and spinal cord NTE were indistinguishable but in the vivo discrepancy between inhibition of brain and spinal cord NTE was matched by a similar discrepancy in inhibition of AChE. It appears that ataxia arises from inhibition of spinal cord NTE and that only in the present compounds (among about 200) was the effect in brain a less than perfect biochemical monitor. 6 references. (Author abstract modified)

002872 Jus, A.; Jus, K.; Fontaine, P. Centre Hospitalier Robert Giffard, 2601 de la Canardiere, Beauport, Quebec G1J 2G3, Canada **Long term treatment of tardive dyskinesia.** Journal of Clinical Psychiatry. 40(2):72-77, 1979.

A 4 year trial to treat tardive dyskinesia by a very slow progressive stepwise diminution of the neuroleptic dose and of the antiparkinsonian agent, as well as by administration of small slowly increasing and then decreasing doses of reserpine or haloperidol was conducted in a sample of 62 chronic schizophrenic patients. This treatment program resulted in the disappearance of tardive dyskinesia in 23 patients and improvement in 26 patients, and had no effect in 13 patients. The group of patients with disappearance of tardive dyskinesia had a mean age significantly lower than the other groups. The rationale of this treatment was based on the concept of desensitization by a slow progressive unblocking of dopaminergic receptor sites. The rabbit syndrome, another tardive neuroleptic side effect, was successfully treated in an additional seven patients by antiparkinsonian drugs. 25 references. (Author abstract)

002873 Klawans, Harold L. Dept. of Neurological Sciences, Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL **Levodopa-induced psychosis.** Psychiatric Annals. 8(9):19-20, 27-29, 1978.

The origins and treatment of levodopa-induced psychosis are described, and the use of levodopa -- either alone or in combination with carbidopa -- in the treatment of parkinsonism is discussed. Levadopa-induced psychosis can occur in two separate clinical situations -- early in the course of treatment, when it can occur in patients with a previous history of mental disease, and after several years of treatment, when it occurs in patients with no previous history of psychiatric disorders. The levodopa-induced exacerbation of preexisting schizophrenia has been observed in two patient populations, the nonparkinsonian patient receiving neuroleptics and the parkinsonian patient not receiving neuroleptics. It is noted that about one third of the patients on levodopa for 2 or more years develop hallucinations. A glossary of terms associated with neurotransmission is provided.

002874 Klawans, Harold L.; Falk, David K.; Nausieda, Paul A.; Weiner, William J. Dept. of Neurological Sciences, Rush Presbyterian St. Luke's Medical Center, 1725 West Harrison Street, Chicago, IL 60612 **Gilles de la Tourette syndrome after long-term chlorpromazine therapy.** Neurology. 28(10):1064-1066, 1978.

Following cessation of 6 years of continuous chlorpromazine therapy for schizophrenia, a young woman developed multifocal tics and vocalizations characteristic of Gilles de la Tourette syndrome. The symptoms were only partially ameliorated by chronic haloperidol therapy. Because of her age and past history, these symptoms were attributed to chronic neuroleptic therapy analogous to neuroleptic-induced tardive dyskinesia, rather than to Tourette syndrome per se. These symptoms suggest that chronic receptor site blockade can result in hypersensitivity of dopamine receptor sites, and that this may play a role in the pathophysiology of Gilles de la Tourette syndrome. 25 references. (Author abstract modified)

002875 Lavan, John N. no address **Medication in the elderly.** Irish Medical Journal (Dublin). 71(5):136-137, 1978.

The prevention of adverse reaction to medication in elderly people is examined. It is suggested that the elderly person is particularly subject to errors of intake as the result of poor comprehension of instructions, blindness, or deafness, especially when multiple dose preparations are used. It is argued that the elderly patient has a reduced physical, psychological, and mental reserve which may impair his ability to withstand drug therapy. An older person's inability to excrete drugs efficiently is discussed. It is concluded that during essential therapy, it may be necessary to reduce dosage so that cumulative side-effects will not occur. 10 references.

002876 Martin-du Pan, R.; Baumann, P.; Magrini, G.; Felber, J.-P. Clinique psychiatrique universitaire de Lausanne, CH-1008 Prilly-Lausanne, Switzerland **Neuroendocrine effects of chronic neuroleptic therapy in male psychiatric patients.** Psychoneuroendocrinology (Oxford). 3(3/4):245-252, 1978.

The neuroendocrine effects of neuroleptic therapy, including hypogonadism with impotence, decreased libido, and oligospermia, were studied in male psychiatric patients. Testosterone levels were within the normal range. Prolactin (PRL) levels were only elevated in patients also receiving anticholinergic agents. A significant inverse relationship was found between the PRL and testosterone levels. Human chorinonic gonadotrophin (HCG) produced a net increase in prolactin and testosterone. The same treatment did not affect the prolactin levels when the patients were treated with bromocriptine (7.5mg b.d), a dopamine agonist. Bromocriptine did not affect the PRL and testosterone levels. 41 references. (Author abstract)

002877 Nejmeh, Maha; Pilpel, N. Dept. of Pharmacy, Chelsea College, University of London, Manresa Road, London, W3 6LX, England **The effect of the photodecomposition of chlorpromazine on lecithin monolayers.** Journal of Pharmacy and Pharmacology (London). 30(12):748-753, 1978.

Chlorpromazine hydrochloride (CPZ) decomposed when irradiated with ultravilet light, forming hydrogen ions, hydrochloric acid, chlorpromazine sulphoxide, and 2-hydroxypromazine. The order of the reaction (as measured by the expansion produced in a lecithin/CPZ monolayer) varied between 0 and 0.75. Results are discussed in relation to the adverse side-effects observed in patients treated with CPZ. 22 references. (Author abstract modified)

002878 Nordgren, Ingrid; Bergstrom, Monica; Holmstedt, Bo; Sandoz, Marianne. Dept. of Toxicology Swedish Medical Research Council, Karolinska Institutet, Fack, S-104 01 Stockholm, Sweden **Transformation and action of metrifonate.** Archives of Toxicology (Berlin). 41(1):31-41, 1978.

The action of metrifonate was studied with mice. Chemical formation of dichlorvos (2,2-dichlorovinyl dimethyl phosphate) was found to occur in mouse brain after i.p. injection of metrifonate (2,2,2-trichloro-l-hydroxyethyl dimethyl phosphonate). A mass fragmentographic technique was used. Different isotopic variants were used both as internal standards and to compensate for dichlorvos formed during the workup procedure. The dichlorvos formed in vivo was found to have its maximal concentration a few minutes after the maximum of the metrifonate itself. The effect of metrifonate and dichlorvos on acetylcholine levels, acetylcholinesterase activity, and synthesis rate of acetylcholine in mouse brain was also studied. In all three cases the effect of metrifonate was found to be prolonged and delayed as compared to the effect of dichlorvos. It is concluded that metrifonate acts as a slow release formulation in the body giving rise to dichlorvos nonenzymatically. This circumstance at least partly explains its efficacy in the treatment of schistosomiasis. 43 references. (Author abstract modified)

002879 Nutt, John G.; Rosin Arnold; Chase, Thomas N. Dept. of Neurology, University of Oregon, Health Sciences Center Portland, OR 97201 **Treatment of Huntington disease with a cholinergic agonist.** Neurology. 28(10):1061-1064, 1978.

The effect of a direct cholinergic agonist, arecoline, was studied in six Huntington disease patients to investigate the hypothesis that the involuntary movements of Huntington disease may be related to cholinergic hypofunction in the striatum. Rather than improving the chorea, arecoline tended to exacerbate the choreic movements. Arecoline did produce significant alterations of blood pressure, heartrate, and body temperature, probably by central cholinergic stimulation. 14 references. (Author abstract modified)

002880 Pandurangi, A. K.; Anatth, J.; Channabasavanna, S. M. National Institute of Mental Health and Neuro Sciences, Bangalore, India **Dyskinesia in an Indian mental hospital.** Indian Journal of Psychiatry (Poona). 20(4):339-342, 1978.

The relationship of old age, edentulous state, previous neurological illness, and neuroleptic drugs to tardive dyskinesia (TD) were examined in 403 hospitalized patients. Tardive dyskinesia is defined as involuntary, repetitive, purposeless, or semipurposive movements of any part of the body. Twenty patients were found to have TD and 18 of these were patients who had been hospitalized for more than 2 years. Seventeen of the patients with TD had been diagnosed as schizophrenics and the other three were epileptic psychotics. It was found that females develop TD more often than men and that the older age group manifests it more often. It is concluded that none of the variables were found to make a statistically significant difference. 9 references.

002881 Port, Friedrich K.; Kroll, Phillip D.; Rosenzweig, Jonathan. V.A. Hospital, 2215 Fuller Road, Ann Arbor, MI 48105 **Lithium therapy during maintenance hemodialysis.** Psychosomatics. 20(2):130-131, 1979.

A case report of the use of lithium carbonate in a patient with severe renal failure is presented. Within 2 months after starting hemodialysis, the patient developed a classic manic psychosis, which included euphoria and paranoia. Evaluation of the patient when lithium was initiated showed moderate depression. After weeks of treatment, the patient was euthymic. Results show that lithium carbonate can be safely administered in the setting of renal failure and hemodialysis if serum lithium concentrations are closely monitored. It is noted that the known dangers of toxicity from lithium carbonate therapy appear to correlate well with serum levels even in the presence of renal failure. 7 references.

002882 Remick, Ronald A.; Fine, Stuart H. Shaughnessy Hospital, 4500 Oak Street, Vancouver, British Columbia V6H 3N1, Canada **Antipsychotic drugs and seizures.** Journal of Clinical Psychiatry. 40(2):78-80, 1979.

Clinical considerations relating to antipsychotic drug use in patients with seizure disorders or seizure susceptibility are addressed. While research on the convulsant properties of antipsychotic drugs in humans is still limited, the differential effects on dopaminergic and cholinergic transmission may be important in determining the relative convulsant effects of neuroleptics. Chlorpromazine, the most widely used antipsychotic, is also the most commonly implicated in precipitation of seizures. On the basis of existing knowledge about seizures and antipsychotics, guidelines for treatment of seizure susceptible children and adults with antipsychotic drugs are presented. It is concluded that in general, polypharmacy should be avoided when possible, dosage increases or decreases should be gradual, treatment of the psychosis should be primary, chlorpromazine should be

avoided when possible, and thioridazine is a good choice in treatment of seizure susceptible psychotic children. 28 references.

002883 Rodstein, M.; Oei, L. S. Jewish Home and Hospital for Aged, 120 West 106th Street, New York, NY 10025 **Cardiac side effects of tricyclic antidepressants in the aged.** Gerontological Society: 31st Annual Scientific Meeting. 18(5, Part 2):117, 1978.

A summary of a paper read at the 31st Annual Meeting of the Gerontological Society, held in Dallas, November 1978, is presented. The nature and frequency of cardiac side-effects from long-term administration of tricyclic antidepressant drugs in usual doses in the aged were studied. Thirty-two subjects, average age 81 years, were followed for an average of 38.6weeks. Ten subjects received amitryptaline in daily dosage from 20 to 75mg for an average of 53 weeks. Two developed side-effects, one inversion of the T-waves, the other electrocardiographic evidence of acute coronary insufficiency. Twenty-one cases received imipramine in daily dosages of 20 to 100mg over an average of 40 weeks. Three developed major side-effects, i.e.,one intermittent left bundle branch block, one acute coronary insufficiency with node dysfunction, and another T-wave inversion and sinus tachycardia. Another developed tachycardia only. One subject developed acute myocardial infarction after two 10mg doses of nortryptaline. Five of the seven cases with cardiac side-effects had prior organic heart disease. It was concluded that the incidence of cardiac side-effects in aged individuals given tricyclic antidepressants over a prolonged period, in usual therapeutic doses, is great enough to warrant frequent careful monitoring of their cardiac status while under therapy. (Author abstract modified)

002884 Rosenblatt, Sidney; Hershman, Jerome M.; Marder, Stephen; Garai, Thomas. Dept. of Endocrinology, Wadsworth V. A. Hospital, Los Angeles, CA 90073 **Chronic phenothiazine therapy does not increase sellar size.** Lancet (London). 2(8084):319-320, 1978.

To investigate whether chronic phenothiazine therapy produces pituitary enlargement, sellar remodeling, and hypopituitarism through lactotroph hyperplasis, serum prolactin concentrations in 21 male patients on long-term phenothiazine therapy were measured, and the lateral sellar surface area of the pituitary was calculated. There was no significant increase in sellar size during mean period of 101 months. Also, the correlation between serum prolactin and phenothiazine dose (expressed as chlorpromazine units) was not significant. 8 references.

002885 Rosenfeld, Alvin A. Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305 **Depression and psychotic regression following prolonged methylphenidate use and withdrawal: case report.** American Journal of Psychiatry. 136(2):226-228, 1979.

A case of severe depression and psychotic regression following prolonged methylphenidate use and withdrawal is reported in a 9-year-old boy. The patient was first evaluated because of depression, dependency, and suicidal ruminations. He had been taking methylphenidate for over 3 years following an initial diagnosis of hyperactive syndrome with psychoneurotic symptoms and personality traits. At the age of 8 the patient began a twice weekly course of psychotherapy. Withdrawal of medication by the parents resulted in a transient disorder of psychotic proportions accompanied by extreme overactivity. The disturbance lasted about a week and resolved spontaneously. Since withdrawal of the medication the patient has functioned well in both the home and school situations, has become more social, and has had no recurrence of depression or suicidal ideation, although serious anxiety continues to be a problem. 5 references.

002886 Schlauch, Robert. Westwood Lodge, 45 Clapboardree Street, Westwood, MA 02090 **Hypnopompic hallucinations and treatment with imipramine.** American Journal of Psychiatry. 136(2):219-220, 1979.

A case of hypnopompic hallucinations in a 61-year-old female treated with imipramine (150mg, h.s.)for endogenous depression is described. After 6 weeks of treatment with imipramine, the patient reported vast improvement in her affect and functioning, but also noted the occurrence of frightening hallucinations during nighttime awakenings. Reduction of the dose to 100mg failed to alleviate the hallucinations, which increased in frequency from about two to four a week. A further reduction in medication to 50mg resulted in the disappearance of the hallucinations, but the reappearance of depressive symptoms. The dose was increased to the original level. Hallucinations gradually decreased to about once a month. A possible relationship between hypnopompic hallucinations and the mode of actions of imipramine in treatment of depression is discussed, and implications of hallucinations for patient noncompliance are noted. 8 references.

002887 Serby, Michael; Angrist, Burton; Lieberman, Abraham. Bellevue Psychiatric Hospital, 400 E. 30th Street, New York, NY 10016 **Mental disturbances during bromocriptine and lergotrile treatment of Parkinson's disease.** American Journal of Psychiatry. 135(10):1227-1229, 1978.

The occurrence of mental disturbance as a side-effect of bromocriptine and lergotrile therapy for Parkinson's disease was investigated. Between 1974 and 1977, 81 patients with advanced Parkinson's disease were treated with bromocriptine, lergotrile, or both agents. Of the 66 patients treated with bromocriptine, 17 developed mental changes. Five of the patients required additional psychiatric treatment for the mental changes, 14 required discontinuation of the drug, and three patients experienced transient changes which disappeared upon reduction of the dose. Among the 53 patients treated with lergotrile, 14 developed mental disturbances. In 12 of these patients, the mental effects necessitated discontinuation of the drug, and additional psychiatric treatment was required in five cases. 10 references.

002888 Shader, Richard I.; Weinberger, Daniel R.; Greenblatt, David J. Psychopharmacology Research Laboratory, Harvard Medical School, Massachusetts Mental Health Center, 74 Fenwood Road, Boston, MA 02115 **Problems with drug interactions in treating brain disorders.** Psychiatric Clinics of North America. 1(1):51-69, 1978.

The interactions involving anticonvulsant and psychotropic drugs are examined and the effect these drugs have on the treatment of patients with impaired central nervous system functions is discussed. Included in the list of anticonvulsants examined are phenobarbital, primidone, carbamazepine, and clonazepam. It is noted that certain psychotropic drugs may interact with phenytoin and other hydantoin derivatives. Psychotropic drug interactions that are considered include tricyclic antidepressants, lithium carbonate, and various sedative hypnotics. It is concluded that since anticonvulsant and psychotropic drugs often do have complex drug interactions, knowledge of these interactions is indispensable in order to employ a rational polypharmaceutical regimen. 93 references.

002889 Sion, Lee. University of Southern California **An experimental study of the longitudinal effects of a methadone treatment program on the personality structure of heroin addicts. (Ph.D. dissertation).** Dissertation Abstracts International. 39(5):2524-B, 1978. (Not available from Univ. Microfilms), 1978.

The effects of a methadone treatment program upon the personality of heroin addicts was studied in 59 male subjects. Subjects were administered the MMPI, and differences within and between experimental and control groups, on pretest and posttest measures, were compared via 42 T-tests. Ten additional comparisons were performed utilizing the nonparametric Mann Whitney U Test. Results show that addicts exhibit significantly more signs of hypochondriasis, depression, and psychopathic deviancy, and less sensitivity and femininity of interests, than do nonaddicts (control). Pretest and posttest within group comparisons yielded no significant differences. It is concluded that methadone treatment does not affect positive personality change in heroin addicts. (Journal abstract modified)

002890 Snider, Gordon B.; Gogate, Shashi A. Lancaster County Hospital, 900 E. King, Lancaster, PA 17602 **Clinical observations following papaverine therapy.** Ohio State Medical Journal. 74(9):571-573,1978.

A description of suspected hepatotoxic reaction to papaverine hydrochloride is presented with clinical data for two patients who developed anorexia, jaundice, and fever 4 to 5 weeks after drug initiation. The patients both in their seventies, developed a hypersensitivity reaction to papaverine hydrochloride which was verified by laboratory evidence of hepatotoxicity, eosinophilia, and liver biopsy verification of the process. The cessation of the patients' papaverine therapy caused dramatic improvement in their clinical course. Subsequent laboratory studies indicated that the hypersensitivity state no longer existed. It is suggested that patients receiving this medication should be monitored closely for evidence of hypersensitivity reaction and hepatotoxicity. 8 references. (Author abstract modified)

002891 Spiker, Duane G. University of Pittsburgh School of Medicine, Pittsburgh, PA 15261 **The toxicity of tricyclic antidepressants.** Communications in Psychopharmacology (Oxford). 2(5):419-427, 1978.

At the Symposium on the Plasma Level Monitoring of Tricyclic Antidepressants held in Vienna in July 1978, the relationship of plasma levels of tricyclic antidepressants (TAD) to cardiovascular and central nervous system toxicity is reviewed and areas requiring further investigation are summarized. The major toxic effects of TAD overdoses and the work of Bigg and associates on validating the clinical diagnosis of TAD overdose with measurement of plasma TAD levels are covered. The following areas for further investigation are addressed: the relationship between cardiac contractility and TAD plasma level, comparison of physostigmine versus digoxin on the decreased cardiac contractility, effect of physostigmine on seizure threshold, the relative toxicity of TAD, and the effect of other drugs on the rate of metabolism of TAD. 61 references.

002892 Van Putten, Theodore. Brentwood Veterans Administration Hospital, Los Angeles, CA 90073 **Lithium-induced disabling tremor.** Psychosomatics. 19(1):27, 31, 1978.

Production of disabling tremor by lithium carbonate was documented by studying 46 patients with manic-depressive illness. All patients were given the drug at conventonal maintenance levels ranging between 0.6and 1.1mEq/liter. All patients were examined for essential tremor before therapy, using the criteria of postural hand tremor since early adulthood, family history of postural tremor, and no evidence of other neurological disease. Six patients developed disabling postural tremors. Each of these patients had either a preexisting essential (heredofamilial) tremor or a family history of essential tremor. It was concluded that lithium exacerbates essential tremor. 8 references. (Author abstract modified)

002893 Veits, Harold R. Dept. of Psychiatry, Naval Regional Medical Center, Camp Lejeune, NC 28542 **Haloperidol encephalopathy: case report.** Military Medicine. 143(3):201-202, 1978.

A case history, which illustrates the clinical, physical, and laboratory manifestations of haloperidol encephalopathy, is presented. Clinically, the patient appeared lifeless, apathetic, and withdrawn and evidenced recent memory impairment. On physical examination, there was mydriasis, tachycardia, hypokinesis, and muscular rigidity. A diffuse slowing of delta waves was noted with continued administration of haloperiol. Discontinuance of haloperidol resulted in clinical improvement in the patient's condition. It is concluded that this encephalopathy may be easily overlooked, as the patient's clinical appearance resembles that of the chronic ""backward" patient. 11 references.

002894 Vohland, H.-W.; Streichert, B. Institut fur Toxikologie und Pharmakologie der Philipps-Universitat, Pilgrimstein 2, D-3500 Marburg a.d. Lahn, Germany **/On the toxicology of carbromal. IV. Binding of carbromal and its narcotically active metabolites to human plasma proteins./** Zur Toxikologie von Carbromal. IV. Proteinbindung von Carbromal und seinen narkotisch wirksamen Metaboliten beim Menschen. Archives of Toxicology (Berlin). 41(1):69-77, 1978.

The binding of carbromal and its metabolites bromoethylbutyramide and ethylbutyrylurea to human plasma proteins was investigated in vitro by use of Sephadex gelfiltration, equilibrium dialysis, and ultrafiltration. No differences appeared in the binding characteristics of human plasma and of human albumine. Proteinbinding of ethylbutyrylurea was found to be less than 5%. Protein binding of carbromal, bromoethylbutyramide, their chlorinated analgous compounds, chloroethylbutyrylurea and chlorethylbutyramide, and of ethylbutyrylurea is strongly correlated to the partition coefficients of these compounds between n-octanol and water, indicating that the intensity of protein binding depends on the hydrophobic character of the substances tested. 23 references. (Author abstract modified)

002895 Weiner, William J.; Nausieda, Paul A.; Klawans, Harold L. Dept. of Neurology, Rush Medical College, 1753 West Congress Parkway, Chicago, IL 60612 **Methylphenidate-induced chorea: case report and pharmacologic implications.** Neurology. 28(10):1041-1044, 1978.

A case report of a child with minimal brain dysfunction whose chorea was found to be related to the major central effect of methylphenidate on central catecholaminergic systems, is presented. Animal research indicating that chronic administration of methylphenidate leads to hypersensitivity of receptor sites is cited. It is hypothesized that chorea beginning shortly after initiation of methylphenidate therapy probably is related to the central dopaminergic effect of the drug and that when choreic movements appear after chronic methylphenidate administration, altered responsiveness of striatal dopamine receptor sites may be responsible. 27 references. (Author abstract modifeid)

002896 West, Rosemary R.; Newgreen, David B. Kingsbury Training Center, Bundoora, Victoria, Australia **Concurrent haloperidol withdrawal and benztropine overdose: a case report.** Comprehensive Psychiatry. 19(6):557-560, 1978.

A case report is presented of severe neurologic symptoms of a choreiform nature occurring following the abrupt accidental cessation of haloperidol and its substitution by large doses of benztropine in a 14-year-old schizophrenic who had been on moderate doses of neuroleptics for 11 years. The course of the disorder is described and the possible causes discussed, together with a review of the relevant literature. The case highlights the potential danger of long-term neuroleptics. The risk of causing

permanent damage to the basal ganglia leading to irreversible tardive dyskinesia must be weighed against the benefits of the medication. 14 references.

16 METHODS DEVELOPMENT

002897 Bailey, David N. Div. of Clinical Pathology, University of California Medical Center, 225 West Dickinson St., San Diego, CA 92103 **Evaluation of drug interferences in the ultraviolet spectrophotometric analysis of plasma theophylline. (Unpublished paper).** Research Report, NIMH Grant MH-30943, 1978. 4 p.

Commonly used drugs (N=45) were evaluated for potential interference in the ultraviolet spectrophotometric analysis of theophylline and an alternate extraction procedure, which was found to eliminate some of the demonstrated interferences, is presented. Eighteen compounds interfered when extracted from plasma at a concentration of 20mg/liter and back-extracted into 0.1N NaOH: group A -- dicoumarol, gentamicin, methyclothiazide, nitrofurantoin, oxyphenbutazone, phenylbutazone, probenecid, and sulfisoxazole; group B -- acetaminophen, 1,7-dimethylaxanthine (caffeine metabolite), dyphylline, furosemide, sulfadiazine, sulfadimethoxine, sulfamethoxazole, theobromine, thiopental, and wartarin. Theophylline could be measured free from interference by the drugs in group A but not group B when back extraction into 1N hydrochloric acid (HCl) was performed. Of 1750 theophylline analyses done by the Jatlow method for 600 different patients during 1976 to 1977, 1.8% of analyses (3.7% of patients) showed interference from one or more of the drugs listed above: sulfamethoxazole (as Spectra or Bactrim) in 50% of cases, furosemide (Lasix), probenecid (Benemid), acetaminphen (Tylenol), gentamicin, and nitrofurantoin (Macrodantin). 24 references. (Author abstract modified)

002898 Bobon, D. P. Department of Psychiatry, Rue Saint-Laurent 58, B-4000 Liege, Belgium, EEC **Time-blind evaluation of psychopathology in drug research.** Acta Psychiatrica Belgica (Bruxelles). 78(4):635-645, 1978.

The usefulness of audiovisual techniques in drug research in psychopathology is discussed and results of experiments are reported. Such techniques avoid time related biases in drug evaluation. Steps in the development of a time blind evaluation procedure include the tape recording of interviews, standardization of the interview, elimination of questions endangering a time blind analysis, and evaluation of different interviews with the same patients at different sessions. Findings from three drug trials using the procedure are reported to demonstrate its effectiveness. 27 references. (Journal abstract modified)

002899 Nagai, Toshiaki; Momose, Takato; Ishiyama, Ikuo. no address **An attempt to detect amphetamine from sweat.** Acta Criminologiae et Medicinae Legalis Japonica (Tokyo). 44(2):88, 1978.

A summary of a paper read at the 14th Annual Meeting of the Japanese Association of Criminality, held in Tokyo, November 1977, is presented. The detection of amphetamine (Methamphetamine) in sweat for use in forensic medicine was studied. The gas chromatographic examination of the extract (PEG 6000) showed a typical peak corresponding to the drug and the mass spectrographic investigation revealed that the peak was that of methamphetamine. The sweat, which was collected 1 hour after the oral administration of 10mg amphetamine, contained a considerable amount of the drug. In some cases, amphetamine in the sweat could be detected even 5 days after oral dose of 10mg. It is concluded that sweat as a specimen is as useful as urine for criminological and/or toxicological investigation of an amphetamine addict. (Journal abstract modified)

002900 Pandey, Ghanshyam N.; Baker, Joyce; Chang, Sidney; Davis, John M. Illinois State Psychiatric Institute, 1601 W. Taylor Street, Chicago, IL 60612 **Prediction of in vivo red cell/plasma Li ratios by in vitro methods.** Clinical Pharmacology and Therapeutics. 24(3):343-349, 1978.

Two incubation procedures were used for the determination, in vitro, of the steady state Li ratio between red cells and external media. The Li ratio in vitro determined prior to Li therapy correlated significantly with the subsequent ratio in vivo between red cells and plasma in patients treated with Li. The Li ratio determined in vitro in patients during Li therapy was significantly higher than the value determined during the pretreatment drug free period, but correlated significantly with Li ratios in vivo. The in vitro procedure used thus could be applied in the prediction of the in vivo Li ratio, and possibly of the response to Li in patients before treatment is begun. It is suggested that it could also be used for studies on abnormalities and on the genetics of Li transport in affective illness. 29 references. (Author abstract)

002901 Pearson, John; Goldstein, Menek; Brandeis, Leslie. Dept. of Pathology and Psychiatry, New York University Medical Center, New Bellevue Hospital, New York, NY 10016 **Tyrosine hydroxylase immunohistochemistry in human brain.** Brain Research (Amsterdam). 165(2):333-337, 1979.

Catecholaminergic neurons were mapped in autopsied human brain, using an antibody to human tyrosine hydroxylase in conjunction with the peroxidase/antiperoxidase technique. In brains from previously healthy males dying of gunshot wounds to the chest, (age 4, 25, and 50 years old), catecholaminergic neurons were found corresponding to most of the AI-AII groups originally described in rat using catecholaminergic fluorescence. No equivalent for the A3 group was found, however. Work in progress indicates that antibodies to other neurotransmitter synthetic enzymes will also react specifically with human cadaver brain. 16 references.

17 MISCELLANEOUS

002902 Adler, Rolf H. Medical Division Lory, Inselspital, Berne, Switzerland **Psychotropic agents in the management of chronic pain.** Journal of Human Stress. 4(2):13-17, 1978.

Psychotropic drugs as agents in the management of chronic pain are reviewed. The phenothiazines, the antidepressants, carbamazepine, and combinations of these drugs are discussed with respect to their mechanism of action, indications, side-effects, and dosages. Uses of psychotropic agents in the treatment of trigeminal neuralgia, postherpetic neuralgia, and cancer pain are described. Problems in the assessment of analgesic effects are considered. 42 references. (Author abstract modified)

002903 Albrecht, Howard Edward. Saint Louis University **Physicians' accuracy in assessing psychiatric patients' symptoms and the appropriateness of their psychotropic drug prescribing. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 7800468, HC$15. MF$7.50. 150 p. 1977. -

The relationship between accuracy in symptom assessment and appropriateness in drug treatment decisions was examined under clinical conditions of varying ambiguity within different diagnostic groups. Subjects were 18 third year medical students nearing completion of an 8 week psychiatry rotation, six second year psychiatry residents and six third year psychiatry residents. Great variance in subjects' symptom accuracy was observed when they diagnosed depressed and psychotic patients presenting symptom pictures of high and low ambiguity; nevertheless the subjects converged on the same medication. No relationship was found between accuracy in symptom assessment and either the decision to prescribe a drug or choice of the appropriate drug prescription. Further, in none of the patient conditions was a relationship found between accuracy in symptom assessment and appropriate amount of drug. It is suggested that the process of drug prescription often may not proceed along logical lines of decision-making; subjects who made appropriate drug treatment decisions may have proceeded directly from specific raw data coues to prescription without transition to symptomology. (Journal abstract modified)

002904 Asberg, Marie; Sjoqvist, Folke. Department of Psychiatry, Karolinska Hospital, S-104 01 Stockholm, Sweden **On the role of plasma level monitoring of tricyclic antidepressants in clinical practice.** Communications in Psychopharmacology (Oxford). 2(5):381-391, 1978.

At the Symposium on the Plasma Level Monitoring of Tricyclic Antidepressants held in Vienna in July 1978, problems and considerations in monitoring plasma levels of tricyclic antidepressants were discussed. There are complexities involved in relating pharmacokinetic and pharmacodynamic data to clinical effect of antidepressant drugs. The following reasons for absence of a relationship between plasma levels of a drug and its therapeutic effect were discussed with reference to the drugs nortriptyline and imipramine: the drug effect is small and/or obscured by other factors; insensitive assessment methods, chemical or clinical; unusual shape of plasma level effect relationships; the plasma level range is too small in the patient sample studied; plasma levels do not reflect drug levels at receptor sites; active metabolites; and the drug is ineffective in the patient group studied. The question of whether plasma level monitoring should be introduced into routine clinical practice is discussed. 43 references.

002905 Ayd, Frank J., Jr. 912 West Lake Avenue, Baltimore, MD 21210 **Haloperidol: twenty years' clinical experience.** Journal of Clinical Psychiatry. 39(11):807-814, 1978.

Current knowledge of the assets and liabilities of haloperidol are reviewed. Technique of therapy, adequate individualized doses, parenteral therapy, cardiovascular effects, extrapyramidal side-effects and interaction with other drugs are discussed. It is concluded that 20 years' clinical experience with haloperidol has verified the efficacy and safety of this neuroleptic when prescribed in adequate individualized dosage for appropriately selected patients. 76 references.

002906 Ban, Thomas A.; Lehmann, Heinz E. Tennessee Neuropsychiatric Institute, 1501 Murfreesboro Road, Nashville, TN 37217 **Uses and abuses of psychoactive drugs.** Southern Medical Journal. 71(10):1287-1293, 1978.

The use of psychoactive drugs is reviewed, and the effects which progress in psychopharmacology has had on the practice of psychiatry are discussed. Since the introduction of chlorpromazine in 1952, pharmacotherapy has provided treatment to schizophrenic patients with high reliability, great simplicity, and fewer hazards than any other treatment known today. The superiority of pharmacotherapy over other physical treatments, and over individual psychotherapy, group psychotherapy and milieu therapy has been demonstrated. A combination of psychosocial therapy and pharmacotherapy may be more effective than pharmacotherapy alone during the rehabilitation and maintenance phases of treatment. The use of neuroleptics, lithium salts, tricyclic antidepressants and anxiolytic sedatives in the treatment of psychiatric patients are reviewed. Indications, recommended dosages, and possible side effects are discussed. Progress in pharmacology shows that sleeping, feeding, and sexual behavior, or habits, are environmentally conditioned variants of biologic rhythms, which in turn can be regulated. 40 references.

002907 Barnes, T. R. E.; Bridges, P. K. Academic Unit for Clinical Psychopharmacology, Guy's Hospital Medical School, London, England **Advances in drug treatment in psychiatry.** Practitioner (London). 221(1324):513-520, 1978.

A classification of drugs available for treating psychiatric illness by target symptom, which brings together drugs with similar therapeutic effects, even though they may be of different chemical structure, is presented. The four groups of antipsychotic drugs (phenothiazines, thioxanthenes, butyrophenones, and diphenylbutylpiperdines), which have the common action of blockade of dopamine neurotransmission, are discussed. The antidepressants (maprotiline, Mianserin, viloxazine, flupenthixol, and nomifensine) are dealt with. The antianxiety drugs (benzodiazepines and betablocking drugs) are discussed. 44 references.

002908 Bianchine, Joseph R.; Shaw, George M.; Greenwald, James E.; Dandalides, Steven M. Ohio State University College of Medicine, Columbus, OH 43210 **Clinical aspects of dopamine agonists and antagonists.** Federation Proceedings. 37(10):2434-2439, 1978.

At the Annual Fall Meeting of the American Society for Pharmacology and Experimental Therapeutics held in Columbus, August 23, 1977, a paper was presented in which the study of dopamine in disease and normal states and its therapeutic applications are summarized. Dopaminergic activity is of special pharmacologic interest in the basal ganglions, hypothalamus, chemoreceptor trigger zone, and renal and cardiovascular systems. Important therapeutic tools have been provided through

in vitro and in vivo bioassays involving receptor binding, enzyme activation, smooth muscle and neuronal excitation, and modification of animal behavior. However, the maximum benefits that dopaminergic drugs may afford have not yet been realized due to an inadequate understanding of disease processes and a relative lack of specificity of drug action. 78 references. (Author abstract modified)

002909 Blacher, Richard. Tufts University School of Medicine, Medford, MA 02155 **Psychological hazards of drug therapy -- keynote address.** Archives of the Foundation of Thanatology. 7(1):85, 1978.

In a summary of a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, the psychological hazards of drug therapy for dying patients and bereaved persons were discussed. These are the two situations which have traditionally demanded of the physician the greatest sensitivity to the human needs of his patients. In his helplessness, he may turn to medication, but in his anxiety, he may deny the patient's reality and give too little. While some mourners may need some temporary sedation for insomnia, prolonged usage indicates a need to talk with the physician about their difficulties. Interference with the necessary grief work by gratuitously alleviating the painful affects may prevent the satisfactory resolution of the mourning. It is concluded that a prescription for a sedative is not a desirable substitute for the availability of the physician.

002910 Blackwell, Barry. Box 927, Dayton, OH 45401 **Treatment adherence: a contemporary overview.** Psychosomatics. 20(1):27-28, 33-35, 1979.

A contemporary overview of treatment medication adherence is presented. It is noted that two factors have contributed to an interest in adherence: 1) the slackening pace of new drug discoveries has stimulated a desire for better use of existing remedies, and 2) new technology has created the means to discover the fate of drugs by measuring body fluid metabolites. It is suggested that since adherence is the outcome of a complex interaction between patient, physician, disease process, treatment regimen, and therapeutic milieu, there is no simple recipe for routine management. It is contended that efforts toward improved adherence should be aimed at improving patient comprehension of the treatment regimen, adequate attention and supervision from health care professionals, and the patient's independent involvement in treatment without supervision. It is contended that the third goal can be reached only in a section of the total population, and may require special techniques to enhance motivation and skill. It is urged that physicians be willing to relinquish adherence responsibility to the patient, and that this graduated approach to self-management be part of every patient's preparation for discharge. 24 references.

002911 Bourne, S. Adult Department, Tavistock Clinic, London NW3 5BA, England **Doctors, physiotherapists, and placebo pharmacology.** British Medical Journal (London). No.6154:1761-1973, 1978.

Psychological problems discussed during a series of seminars that confront physiotherapists in their relationships with doctors are discussed. The following factors were identified as contributing to their dissatisfaction: doctors misused physiotherapy as a placebo in cases of incurable and untreatable disease and in cases involving mental problems; they avoided knowing the facts about their patients so that they could escape patient questions which went unanswered by the doctor; using quasiscientific apparatus which tended to replace physical contact; a view of their psychological skills as illicit and unprofessional; and an uncertainty about their role as social workers. However, they tended to idealize doctors. They also tended to reinforce sexual stereotyping and the image of physiotherapy as unscientific and intuitive. 9 references. (Author abstract modified)

002912 Breithaupt, H.; Fellmann, A. Zentrum fur Innere Medizin, Abteilungen Klinikstrasse der Univ. Giessen, Giessen, Germany **/Treatment with psychopharmaceutical agents./** Behandlung mit Psychopharmaka (I). Medizinische Welt (Stuttgart). 29(34):1301-1305, 1978.

The effects of psychopharmaceutical agents on the workings of the CNS and their psychological functions are discussed. While psychopharmaceutical agents may be classified in a wide range of functions, three primary types of substances are differentiated: tranquilizers, antidepressants, and neuroleptics. Benzodiazepine and its cumulative long-term tranqulizing effects are described. The functions of various antidepressive psychopharmaceutical agents are discussed as well as their side effects in the treatment of severe depressions. Contraindications of antidepressant drugs are discussed and it is suggested that in schizophrenia the drugs may produce a psychotic breakdown.

002913 Buchanan, Darrell S. Dept. of Psychiatry, Walter Reed Army Medical Center, Washington, DC 20012 **Iatrogenic causes of neurologic disorders: part 1. affect, convulsions, and encephalopathies.** Geriatrics. 33(8):59-64, 1978.

Iatrogenic causes of neurological disorders in the aged are discussed. Drug therapy is more difficult in older people because they have a high incidence of multiple system diseases and a slowdown in metabolic processes. Drugs intended to normalize the depressed or psychotic behavior of an elderly patient may instead cause disturbances in memory and attention, or provoke anxiety. Phenothiazines, chlordiazepoxide hydrochloride, and all the effective drugs for Parkinson's disease can have undesirable side effects. Four tables are presented to list the therapeutic agents that have been implicated in various iatrogenic neurological disorders. 1 reference.

002914 Bunney, William E., Jr.; Pert, Agu; Rosenblatt, Jack; Pert, Candace B. Biological Psychiatry Branch, NIMH, Bethesda, MD 20014 **Some biological considerations of the mode of action of lithium in the treatment of affective illness. (Unpublished paper)** Bethesda, MD, NIMH, 1978. 15 p.

The properties of lithium and four possible sites of interaction between lithium and other cations are discussed. It is emphasized that lithium must interact with specific receptors to produce its therapeutic effects, and it is suggested that lithium interacts with the cyclic/AMP/mediated process. A hypothesis that the onset of mania may be associated with the development of supersensitivity of catecholamine receptors is presented. New evidence is reported that suggests lithium could block the development of supersensitivity in central nervous system neuronal receptors in rats. 39 references.

002915 Burrows, Graham D.; Davies, Brian; Norman, Trevor; Maguire, Kay; Scoggins, Bruce A. Department of Psychiatry, University of Melbourne, Royal Melbourne Hospital, Victoria, 3050, Australia **Should plasma level monitoring of tricyclic antidepressants be introduced in clinical practice?** Communications in Psychopharmacology (Oxford). 2(5):393-408, 1978.

At the Symposium on the Plasma Level Monitoring of Tricyclic Antidepressants held in Vienna in July 1978, thirty-nine studies relating plasma concentrations of antidepressant drugs to clinical response were reviewed. About half of the studies favor various relationships in the eight drugs studied. Possible reasons for the discrepancies are discussed and suggestions for future

studies are outlined. Results of the effects of long-term lithium administration show that the tricyclics will play an important role in maintenance therapy for recurring affective disorders. It is concluded that routine monitoring of plasma levels of tricyclic antidepressants is not warranted. 60 references. (Author abstract modified)

002916 Carr, Robert R. no address **Cocaine today.** Human Behavior. 8(3):43-47, 1979.

An overview of cocaine, an increasingly popular recreational drug (drug of abuse), is presented. The nature of cocaine, its traditional use by the natives of Peru and Bolivia, its legal status and history, and administrative, medical, and legal attitudes toward the use of cocaine are discussed. While in some cases, cocaine can be lethal, in general it has an excellent record for clinical safety. A number of studies have indicated that, depending on route of administration, dosage level, and dosage frequency, side-effects from cocaine use may include transient and generally mild hangover, paranoia, irritability, depression, and sleep disturbance. There has been little evidence for psychological dependence or pharmacological tolerance. Transient perceptual phenomena, pseudohallucinations and tactile hallucinations, and mild confusion and lack of attention have also been reported, generally in association with intensified drug use. Multiple drug use and the association of cocaine with crime and violence are examined; and its use as a sexual stimulant is discussed. Its legal future is also considered.

002917 Cleghorn, R. A. Department of Psychiatry, Sunnybrook Hospital, 2075 Bayview Avenue, Toronto, Ontario M4N 3M5, Canada **The place of lithium and anti-dopaminergic drugs in manic depressive and schizo-affective disorders.** Indian Journal of Psychiatry (Poona). 20(3):237-239, 1978.

The place of lithium and antidopaminergic drugs in the treatment of manic-depressive and schizoaffective disorders is discussed. Diagnostic issues relating to schizoaffective disorders are examined. Hypotheses briefly discussed include that schizoaffective disorders are: a variant of schizophrenia, a variant of affective disorder, a third psychosis differing from both schizophrenia and affective disorder, or a group of psychoses which become recognizable at followup by the clinical picture, course, and family history. Most likely, schizoaffective psychosis is a heterogenous entity. During the acute phase the use of drugs such as phenothiazines and haloperidol is necessary and lithium may also be given. In general, acute symptoms will eventually subside and lithium therapy will be sufficient for symptom control. Occasional reappearance of affective and/or schizophrenic symptoms will require short-term reinstitution of antidopaminergic drugs in addition to lithium. 15 references.

002918 Cohen, Sidney. Department of Psychiatry, University of California at Los Angeles, Los Angeles, CA 90024 **20 years with the major tranquilizers.** Resident & Staff Physician. 24(2):67-71, 75, 1978.

Developments in the use of tranquilizers and antipsychotic drugs such as the phenothiazines, butyrophenones, and thioxanthenes, are discussed in the treatment of psychiatric patients. Recommendations are made for prevention of drug dependence and for proper levels and combinations of psychoactive drug prescriptions. It is asserted that dosages should be more flexible and adapted to specific situations and conditions. Suggestions are offered for controlling and evaluating the impact of side-effects such as depression, tardive dyskinesia, hypotension, and toxic delirial syndromes.

002919 Conde Lopez, V.; Guerro Cerrato, D. no address **/Introduction to the roundtable about ""present psychopharmacological treatment in schizophrenias."/** Introduccion a la mesa redonda sobre ""tratamientos psicofarmacologicos actuales en las esquizofrenias." Acta Luso-Espanolas de Neurologia, Psiquiatria y Ciencias Afines (Madrid). 6(3):300-308, 1978.

At the XII Reunion of the Spanish Society of Psychiatry held in Barcelona, May 1977, a paper was presented which discusses the present psychopharmacological treatment of schizophrenia. The importance of neuropharmacology in contemporary psychiatry is emphasized. From the glossary of the VII Revision of the International Classification of Illnesses, a definition of schizophrenia and its characteristics are presented. No universally accepted theory, which integrates all the facts about schizophrenia, has been developed. A brief history of interest and research in neuropharmacology is presented, from the 1950's to the present, in an attempt to integrate existing facts. A psychopathological classification of the various forms of schizophrenia is reviewed. The history of pharmacological discoveries, including the breakthrough of the antipsychotic drugs' ability to block dopamine receptors, is discussed. It is recommended that research be continued to better understand the schizophrenic world. 62 references.

002920 Costa, E.; Guidotti, A. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Recent studies on the mechanism whereby benzodiazepines facilitate GABAergic transmission.** Washington, DC, NIMH, 1978. 13 p.

The influence of membrane proteins on receptor cooperative interaction in GABAergic transmission was investigated. Work is summarized showing that the affinity of recognition sites for GABA is regulated by a modulator protein present in the membrane. Benzodiazepines change the affinity of recognition sites for GABA by interfering with the function of the protein. Preliminary data suggest that phosphorylation of membrane protein may be involved in this regulatory mechanism. 15 references.

002921 Crammer, John; Barraclough, B. M.; Heine, Bernard. no address **The use of drugs in psychiatry.** London, Headley Bros. Ltd., 1978. 225 p.

A discussion of the treatment and management of psychiatric illness with drugs is presented. The clinical use of separate groups of drugs, including tricyclics, thioxanthines, and benzodiazepines, is detailed. The bioavailability of each group of drugs and their interactions are emphasized. An appendix on how to apply electroconvulsive therapy is provided, and a separate index of drugs with approved names and proprietary names is included.

002922 Davy, J. P.; Moulin, M.; Andersson, J. C.; Halbecq, J. J.; Morel, P.; Poilpre, E. Centre Psychiatrique Esquirol, C.H.U. Cote-de-Nacre, F-14033 Caen Cedex, France **/Relation between the levels of neuroleptics and the dosages, the clinical efficacy and the side-effects./** Relation des taux des neuroleptiques avec les doses, les actions therapeutiques et les effets secondaires. Encephale (Paris). 4(4):293-321, 1978.

The relation between the plasma rate of neuroleptics and the dosages, therapeutic action, and secondary effects involved with them was researched to determine the individual difference in the therapeutic response towards medication. For low dosages of neuroleptics, the methodology for quantitation used was mass fragmentation and chromatography; otherwise it was found that the radio-immunological assay had much promise. The plasma rate of the neuroleptics was not correlated with the dosage from one person to another, and it was found that a linear relationship existed for the daily dosages of one individual. Few of the neuroleptics were studied for the correlation between plasma level and therapeutic effect, and while the correlation was un-

certain with nontransformed chlorpromazine and thioridazine, there was a higher correlation with sulphoxyde metabolite and butaperazine. Though the side-effects were well correlated with the plasma levels at the beginning of the therapeutic, the action of tolerance intervened rapidly. On the basis of objective data, the many uncertainties explain the difficulty of actual clinical utilization of neuroleptics. 137 references.

002923 Denden, D. J. no address **Cholinergic mechanisms and psychopharmacology.** Advances in behavioral biology, Vol. 24. New York, Plenum Press, 1978. 885 p. $49.50.

Fifty-six papers, originally presented at a Symposium for Cholinergic Mechanisms and Psychopharmacology, held in La Jolla, CA, March 1977, are compiled. Seven major categories of acetylcholine (AcCh) research are included: attempts to identify cholinergic receptors by enzymatic, histological, biochemical, and pharmacological methods; critiques of assay methods employed for choline (Ch), AcCh and related substances; the interrelationships of AcCh, cAMP, and cGMP; the mechanisms of formation, action, and metabolism of Ch and AcCh; the storage and release of AcCh; modulators of AcCh; and the probable clinical roles of cholinergic function or dysfunction. Essentially all of the studies are status reports of ongoing research, and few definitive conclusions are presented.

002924 Deniker, P.; Poirier, M. F. Centre Hospitalier Sainte-Anne, 1, rue Cabanis, F-75674 Paris Cedex 14, France **/The place of carpipramine among psychotropic drugs./** Place de la carpipramine parmi les psychotropes. Encephale (Paris). 4(5, Supplement):553-567, 1978.

In a paper presented at the Conference on the Concept of Inhibition in Psychiatry, held in Monastir, Yugoslavia, October 1978, methods used to define the place of carpipramine among psychotropics, in accordance with the classification proposed by Delay and Deniker. Discriminant analysis tries to place carpipramine in one of these groups. With the use of this method, it is shown to be impossible to classify 19 psychotropic drugs, carpipramine being one of them. It is concluded that the unique clinical properties of carpipramine prevent its easy classification among other psychotropic agents. 50 references. (Journal abstract modified)

002925 Deniker, P.; Radouco-Thomas, C.; Villeneuve, A.; Baronet-Lacroix, D.; Garcin, F. Hopital Sainte-Anne, Paris, France **Neuro-psychopharmacology.** Oxford, Pergamon, 1978. 932 p. Vol. 1.

The proceedings of the 10th Congress of the Collegium Internationale Neuro-Psychopharmacologicum, held July 1976 in Quebec, are presented. Symposia topics include geriatric neuropsychopharmacology, parameters and methods in the measurement of therapeutic response, international standards in psychopharmacology, training models in psychopharmacology, psychostimulant drugs, drug dependence therapy resistant patients and safety margin problems, synaptic receptors and psychotropic drugs, role of cations in synaptic function, putative neurotransmitters and neuromodulators other than aromatic acids, interrelationships between various neurotransmitter systems, indoleamines and precursors in depression, neurotransmitters and brain dysfunction, genetic psychopharmacology, metabolism and kinetics of psychotropic drugs, and mechanisms of action of minor tranquilizers.

002926 DiGiacomo, Joseph N.; Rosen, Harold. Veterans Administration Hospital, Philadelphia, PA 19104 **Psychosomatic disorders: psychotropic medications.** Psychosomatics. 20(2):95, 101-103, 107, 1979.

The concerns of psychiatric consultation in the management of the patient with psychosomatic disorders are discussed. The most important principle in the use of psychotropic medication is to avoid administering any until a thorough psychologic evaluation has been accomplished. Different conditions that necessitate pharmacologic treatment are described, including severe persistent anxiety, severe persistent pain, and depression. Recommendations for management of psychotropic intervention are presented. 2 references.

002927 Doongaji, D. R.; Bharucha, M. P. E.; Vahia, V. N.; Thatte, Shubha S.; Mistry, P. P.; Pradhan, Meena. Dept. of Psychological Medicine, K. E. M. Hospital and G. S. Medical College, Bombay, India **On placebos, placebo responses and placebo responders. III. Psychological, pharmacological and psychophysiological correlates.** Indian Journal of Psychiatry (Poona). 20(4):324-331, 1978.

The psychological, psychopharmacological and psychophysiological characteristics of placebo responders and nonresponders were examined in 100 normal volunteers. Correlations were sought among the interacting variables. Seventy-two percent of the subjects had baseline symptoms. Placebogenesis was present in 62 subjects. A bidirectional placebo response which is hitherto unreported was obtained in almost 52% of the placebo responders, in addition to positive and negative responses. It is concluded that placebogenesis should be considered whenever clinical evaluations of treatment modalities are to be made. 17 references. (Author abstract modified)

002928 Eichel, Glenn R.; Troiden, Richard R. Warren County Alcohol and Drug Abuse Clinic, 416 South East Street, Lebanon, OH 45036 **The domestication of drug effects: the case of marijuana.** Journal of Psychedelic Drugs. 10(2):133-136, 1978.

The extent to which reported subjective effects of marihuana smoking have changed between the late 1960s and late 1970s was examined utilizing questionnaire responses of 76 sociology students and 99 rock concert and 97 jazz concert attendees (90% return rate). A high rate of usage was found for all three groups: 70%, 90%, and 76& for the three groups respectively. Most frequently reported subjective effects were found to be thirst, mental relaxation, decreased physical tension, increase sexual pleasure, and alterations in time perception. These subjective effect are contrasted with those found in a previous study (Comitas, 1976) of ganja use of Jamaica. Further, data failed to show change over time in perceived effects of marihuana smoking, suggesting that much of the verbal lore growing out of the marihuana using subculture of the 1960s sensitizes users to expectations of drug related experience. Results underscore the importance of role of cultural predispositions and expectations in drug experience. 11 references.

002929 Escala Zerpa, Reinaldo. no address **/The silence of the suspect./** Le silence du suspect. Etudes Internationales de Psycho-Sociologie Criminelle (Paris). No. 31-33:40-48, 1978.

At the inaugural meeting of the ""Crimes and Liberties" Congress at the First Chamber of the Appellate Court of Paris, a paper was presented which discusses the right of silence for the suspect. From a moral and ethical standpoint, there are seven controversial areas: the right to remain silent, the attitude of caution, the attitude of the defendent, narcoanalysis, the polygraph, and the conclusions. Psychologically, the narcoanalysis and the polygraph are important factors. Narcoanalysis is a method of medical exploration to obtain a series of facts that are buried in the subconscious of the individual: it is a psychoanalysis brought about by the injection of a narcotic substance. Many faults are found in narcoanalysis, because it takes away the individual's right to silence, and should only be used with the agree-

ment of the individual. It is suggested that the polygraph should only be used as an aid to complement investigative work, and that the right of the suspect to remain silent be protected as an inviolable right.

002930 Fann, William E.; Wheless, Jeanine C. Dept. of Psychiatry, Baylor College of Medicine, 1200 Maursand Ave., Houston, TX **Dangers of psychotropic polypharmacy.** Current Psychiatric Therapies. 18:143-154, 1978.

The potential dangers of psychotropic polypharmacy are discussed. Interactions of two or more drugs may involve interaction at the plasma protein binding level, impaired gastrointestinal absorption, altered metabolism, altered excretion, blocked transport, and altered mediator activity. Usually, psychiatric patients are initially treated with a single drug, and other drugs are added later either to counteract side-effects or to treat symptoms for which the initial drug is ineffective. The assumption behind this tactic is that smaller doses of two drugs may be more potent and less toxic than a large dose of one drug. However, there are no controlled data to support this hypothesis. It is concluded that polypharmacy should be subjected to controlled investigation. 43 references.

002931 Fuller, Lois B. no address **Heroin analgesia.** Archives of the Foundation of Thanatology. 7(1):43, 1978.

In a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, heroin as an effective analgesic for pain in the terminally ill patient was discussed. Heroin provides excellent analgesia, with the patient remaining alert and with fewer side-effects than morphine, especially nausea and vomiting, and respiratory depression. When the patient is taking heroin, depression rarely becomes a clinical problem. Prolonged usage of morphine and demerol seem to increase depressive symptoms. A patient's depression is frequently difficult to treat when relying on the tricyclic antidepressant drugs, as common side-effects are agitation and sleeplessness, which present yet another treatment problem. With assurance that suffering will be alleviated, the mental status of the patient will improve perceptibly. Control of physical and mental pain go hand in hand. It is concluded that when skillfully performed, drug management contributes greatly to the level of the patient's care and comfort. 5 references.

002932 Gaughan, Lawrence D.; LaRue, Lewis H. Washington and Lee University, Lexington, VA 24450 **The right of a mental patient to refuse antipsychotic drugs in an institution.** Law and Psychology Review. 4:43-85, 1978.

The nature of antipsychotic drugs, justifications for the use of antipsychotic drugs, and justifications for refusal to use antipsychotic drugs are presented as background to a discussion of the right of patients in institutions to refuse drugs. The existing legal framework, including involuntary commitment, the adjudication of incompetency, and the nature of the competency evaluation, are discussed. Litigation concerning these issues is reviewed. Little authority is found to support the proposition that aspects of this right exist as a matter of federal constitutional law. It is proposed that an institutionalized mental patient has a general right to refuse antipsychotic drugs; a departmental or hospital policy on refusal of medication and a hospital drug policy (to be posted on each unit) are proposed. The proposed forms are appended. 93 references.

002933 Gochfeld, Linda G. P.O. Box 440, Kingston, NJ 08528 **Drug therapy and modern psychoanalysis.** Modern Psychoanalysis. 3(2):203-216, 1978.

The therapeutic use of drugs in combination with psychoanalysis in the treatment of emotional disorders is discussed. It is suggested that when the following symptoms are severe, disabling, or dnagerous, drugs are recommended: 1) psychotic, disorganized thought or behavior, agitation, delusions, hallucinations, destructive bheavior; 2) severe depression with physiological symptoms; 3) manic-depressive illness with severe mood swings; and 4) phobic anxious syndrome with disabling fears and panic attacks. If combined treatment is to be successful, certain basic psychoanalytic principles must be applied in new ways. Understanding of transference and resistance is extended to the drug therapy transaction, and countertransference is expected and utilized in understanding the situation. It is concluded that the combination of modern psychoanalysis with drug therapy offers new possibilities for the treatment of the seriously ill. 32 references.

002934 Goldberg, Ivan K. New York Psychopharmacologic Institute, 51 East 90th St., New York, NY 10028 **New York Psychopharmacologic Institute.** Archives of the Foundation of Thanatology. 7(1):79, 1978.

In a summary of a paper delivered at a Symposium on the use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosoical Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, the New York Psychopharmacologic Institute, recently incorporated as a nonprofit health care delivery system, is described. institute is a private outpatient service offering assistance to psychotherapists by providing psychopharmacologic treatment for patients with manic depressive disease, other depressions, severe anxiety, disabling phobias, schizophrenia, other psychoses, or chronic pain problems. Members of the staff are experienced in the management of the pain of terminal illness. Additional activities of the Institute include research on the quantification of psychopathology, and programs to further the understanding of psychochemotherapy in the management of mental disorder. It is concluded that psychopharmacologic treatment at the Institute is designed to facilitate rather than replace the patient's psychotherapy.

002935 Goldberg, Ivan K.; DeBellis, Robert; Kutscher, Austin H.; Schoenberg, Bernard. no address **Selected studies of the pain rehabilitation unit: research into controlling pain and anxiety resulting from malignant disease.** Archives of the Foundation of Thanatology. 7(1):76, 1978.

In a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, a pain rehabilitation unit proposed to serve as the locus of research into problems related to the control of pain resulting from malignant disease was discussed. Four studies are proposed: 1) a study designed to identify patients, through the psychophysiologic measurement of anxiety, likely to be most and least responsive to pain control techniques; 2) a study of the possible potentiating effects of antianxiety agents and antidepressants upon the action of analgesics; 3) a study of the role of Levo Dromeran in the care of the cancer patient with pain; and 4) a study of the effects of group psychotherapy upon the cancer patient with pain. It is concluded that the long-term management of the cancer patient in severe pain is a neglected area of research.

002936 Goldberg, Ivan K.; Schoenberg, Bernard; Peretz, David; Kutscher, Austin H.; Kutscher, Harlan A. College of Physicians and Surgeons, Columbia University, New York, NY 10027 **Use of the psychopharmacologic and narcotic agents in the management of the dying patient, anticipatory grief and bereave-**

ment: effectiveness. Archives of the Foundation of Thanatology. 7(1):52, 1978.

In a summary of a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, medical faculty opinion regarding the use of psychopharmacologic and narcotic agents in the management of terminal patients and their families is described. A survey was sent to the chairmen of the departments of Pharmacology, Surgery, Medicine, Psychiatry, and Pediatrics at every medical school in the United States. Each individual was requested to estimate the effectiveness of different drugs in certain clinical situations that are typical during terminal care. Psychopharmacologic treatment of anxiety and depression is frequently judged effective, but not nearly as effective as the treatment of severe pain with narcotics. It is concluded that psychopharmacologic and narcotic agents are basically considered effective tools in the management of the dying patient and, to a lesser extent, in the management of his relatives.

002937 Gram, Lars F. Department of Clinical Pharmacology, Institute of Pharmacology, Odense University, J.B. Winslows Vej 19, DK-5000 Odense C, Denmark **Plasma level monitoring of tricyclic antidepressants: methodological and pharmacokinetic considerations.** Communications in Psychopharmacology (Oxford). 2(5):373-380, 1978.

At the Symposium on the Plasma Level Monitoring of Tricyclic Antidepressants held in Vienna in July 1978, the usefulness of plasma level monitoring of tricyclic antidepressants and methodological factors that need to be considered were discussed. Consideration should be given to the need to: standardize the dose sampling, blood sampling schedule to insure that absorption and distribution take place before plasma levels are monitored; consider interindividual differences in plasma protein binding that might necessitate measurement of free drug concentration; determine whether there are active metabolites and their relative potency; consider objective measurements of drug compliance; and determine the relationship between drug levels and clinical effects. 29 references. (Author abstract modified)

002938 Halberstam, Michael. 2520 L St. NW, Washington, DC 20037 **An office study of patient attitudes toward tranquilizing medication.** Southern Medical Journal. 71(2):15-17, 1978.

The attitudes of 50 office patients toward taking tranquilizers were examined in a paper presented at the McLean Hospital Symposium held in Dallas, November 1977. A simple study involving verbal responses to a direct question is offered as an indication that patients can be skeptical and resistant to being tranquilized. Suggesting the use of minor tranquilizers on a temporary, situational basis is offered as a method to overcome patient hostility toward tranquilizers. Helping people identify the situations which tend to produce anxiety and premedication with a minor tranquilizer is suggested. 2 references.

002939 Hartelius, Hans; Larsson, Anna-Kerstin; Lepp, Marje; Malm, Ulf; Arvidsson, Annie; Dahlstrom, Hans Psychiatric Dept., Centralsjukhuset, S-291 85 Kristianstad, Sweden **A controlled long-term study of flunitrazepam, nitrazepam and placebo, with special regard to withdrawal effects.** Acta Psychiatrica Scandinavica (Kobenhavn). 58(1):1-15, 1978.

The hypnotic and withdrawal effects of flunitrazepam, nitrazepam, and a placebo were studied in 117 outpatients using hypnotics for at least 3 months prior to the study. The 13 week trial period consisted of 3 weeks on the previously used hypnotic, 3 weeks on a test drug, and 4 weeks of observation after a request to stop medication with the test drug. The effects were evaluated every week by self-ratings. Also noted were: the frequency of dose increase after 1 week of the test period, number of dropouts in the test period, and failure in the attempt to stop taking the test drug. A psychological concentration test was done, as was a followup interview. It is concluded that withdrawal of a hypnotic in chronic users is not facilitated by the use of a placebo. This is interpreted as due to a strong psychological dependence upon the hypnotics and their lack of pharmacological effects during long-term treatment. 14 references. (Author abstract modified)

002940 Henderson, Ian. no address **The use of psychopharmacologic agents including heroin (diacetylmorphine) in the management of the dying patient.** Archives of the Foundation of Thanatology. 7(1):45, 1978.

In a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, several arguments against the use of heroin (diacetylmorphine) for the relief of pain in terminally ill patients were presented. The euphoria produced by heroin is greater than that obtained by morphine. It is faster acting than morphine, but its duration of activity is less. Both psychological and physical dependence are known to occur after relatively short periods of exposure to heroin. In general, dying patients tend to continue their life style attitudes. ""Minimizers" have the capacity to dissociate physical pain from their emotional response to it, and decrease the intensity of stimuli reaching the cerebrum from the thalamus. ""Maximizers" do the opposite. Most analgesics work best in ""maximizers," who start to behave like ""minimizers." It is concluded that the intense euphoria produced by heroin is so rhythmic and relatively short-lived, that it is seldom of much help in the psychological management of the terminally ill.

002941 Henderson, Ian. no address **Commentary on essay by Dr. E. Kubler-Ross.** Archives of the Foundation of Thanatology. 7(1):44, 1978.

In a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, the indiscriminate use of drugs at the time of death as a manifestation of the shortcomings of our civilizations was discussed. Our scientifically and technologically oriented medical education pays no attention to the humanistic and philosophical aspects of disease and death. The unprecedented prolongation of life expectancy has made death unreal for a large percentage of our population. In the past religious belief and a cohesive family structure lent support at a time when man's loneliness and fears were extreme. In this setting, the demands placed on hospital personnel are often unrealistic and therefore disappointing. It is concluded that the use of drugs by the dying patient and his caretakers manifests deficiencies of our present social climate. 1 reference.

002942 Hollister, Leo E. no address **Clinical pharmacology of psychotherapeutic drugs.** New York, Churchill Livingstone, 1978. 240 p. $19.50.

The approach of the clinical pharmacologist, focusing upon pharmacokinetics, pharmacodynamics, drug interactions, and drug effects on biologic processes, is presented. The pharmacologic actions and pharmacokinetic properties of the various drugs in each drug class (antianxiety agents, hypnotics, antidepressants, antipsychotics, and lithium salts) are documented and critically reviewed, and possible clinical implications are assessed. Further clinical perspective is provided in concise dis-

cussions of the pertinent disease and how they can be modified by appropriate pharmacotherapy.

002943 Howard, P. J. Department of Anaesthetics, Queen's University of Belfast, Belfast, Ireland **The stability of diazepam in plasma samples when stored under varying conditions.** Journal of Pharmacy and Pharmacology (London). 30(2):136, 1978.

The effects of storage conditions and length of storage time on the stability of diazepam in human plasma samples were investigated using single stage benzene extraction and gas liquid chromatography. Studies performed on samples stored at minus 20 degrees C for 1 year, at room temperature for 20 days, or at 4 degrees C for 8 weeks reveal no evidence of deterioration of the diazepam. 3 references.

002944 Itil, Turan M.; Reisberg, B.; Simeon, S. Division of Biological Psychiatry, New York Medical College and Veterans Administration Health Care Facility, Montrose, NY **Use of psychotropics in the world.** International Pharmacopsychiatry (Basel). 13(1):39-49, 1978.

In a paper presented at the International Congress on Transcultural Psychiatry, Bradford, England, July 1976, results on a questionnaire on medication preferences for treating psychiatric disorders sent to 1,059 psychiatric drug investigators in 53 countries were reported. Of the 264 questionnaires which were returned, 165 were used. A total of 87 different psychotropic drugs were selected by the respondents. Chlorpromazine was the most frequently cited medication in the treatment of schizophrenia. Amitriptyline and imipramine together accounted for most of the medications chosen for all varieties of depression. In the treatment of mania, chlorpromazine was chosen by almost one third of the sample: lithium was chosen by only one fifth. Chlordiazepoxide and diazepam were equally preferred in treatment of alcoholism. Most psychiatrists preferred not to use any psychotropic medications consistently in treating patients with organic brain syndromes. Implications of the findings were discussed and compared with similar studies in more limited geographical regions and in children. 3 references. (Author abstract modified)

002945 Itil, Turan M.; Seaman, Phyllis. 150 White Plains Road, Tarrytown, NY 10591 **Drug treatment of human aggression.** Progress in Neuro-Psychopharmacology (Oxford). 2(5/6):659-669, 1978.

Antiaggressive and proaggressive properties of a variety of psychotropic and other centrally effective compunds were reviewed. Among the sedative psychotropic compounds, neuroleptics and benzodiazepine anxiolytics are the most frequently used drugs in human aggression and violent behavior. The antiaggressive effects of lithium are an important new finding. The drug of choice for the aggressive state of children and adolescents is predominantly psychostimulants, particularly if the aggression is associated with the minimal brain dysfunction. In episodic outbursts with or without clinical seizures, anticonvulsant drugs should first be tried specifically if patients have abnormal EEG findings. Most of the compounds with antiaggressive properties also possess proaggressive effects. It is suggested that aggression producing effects of benzodiazepine and anxiolytics, antiepileptics and psychostimulants can be very significant in clinical practice. 74 references. (Author abstract modified)

002946 Jospe, Michael. no address **The placebo effect in healing.** Lexington, MA., Lexington Books, 1978. 162 p. $15.95.

An overview of the placebo effect in healing is presented. The empirical literature concerning the placebo effect and recent attribution research are reviewed. It is asserted that attribution research can play a potentially important role in understanding the placebo effect. Three components of the placebo effect are identified as physiological arousal, emotionally relevant cognitive factors, and a perceived causal link between these factors. Methodological problems in placebo research are discussed. Findings concerning the personality and habits of placebo receptors are reported.

002947 Kellner, Robert; Rada, Richard T.; Winslow, Walter W. Department of Psychiatry, University of New Mexico, School of Medicine, Albuquerque, NM 87106 **The psychopharmacologic treatment in bereavement.** Archives of the Foundation of Thanatology. 7(1):50, 1978.

In a summary of a paper delivered at a Symposium on the use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, the lack of research in the area of psychopharmacologic treatment of bereaved persons was discussed. Some feel that bereavement is not an appropriate topic for psychopharmacologic research because it is a normal reaction which is only shortlived. Bereaved people form only a small proportion of the psychiatric clinic population and thus are not easily accessible to the researcher. It is concluded that bereavement itself is not an indication for psychopharmacologic treatment, although treatment may have an important role to play if the distress is unbearable and incapacitating, if psychiatric or psychosomatic complications occur, and if the response to psychotherapy is inadequate.

002948 Kober, Anita; Jenner, Asa; Sjoholm, Ingvar; Borga, Olof; Odar-Cederlof, Ingegerd. Dept. of Pharmaceutical Biochemistry, Biomedical Center, University of Uppsala, Box 578, S-751 23 Uppsala, Sweden **Differentiated effects of liver cirrhosis on the albumin binding sites for diazepam, salicylic acid and warfarin.** Biochemical Pharmacology (Oxford). 27(23):2729-2735, 1978.

The effects of liver cirrhosis on the albumin binding sites for diazepam, salicylic acid, and warfarin were examined and compared to those in normal human serum. The binding of diazepam and salicylic acid was impaired in serum from the patients when compared with the binding in serum from healthy individuals, while the binding of warfarin was unchanged. The results were the same when the binding was studied with albumin isolated from patient serum and normal serum. It is concluded that the decreased binding of diazepam and salicylic acid in the serum from the patients with liver cirrhosis can be related to the presence of allosteric inhibitors specifically affecting the diazepam binding site on albumin, while the warfarin site apparently is unaffected. 42 references. (Author abstract modified)

002949 Kontos, Peter G.; Steinhilber, Richard M. Cleveland Clinic, 9500 Euclid Ave., Cleveland, OH 44106 **Using antidepressants effectively.** Postgraduate Medicine. 64(2):55-57, 60-61, 1978.

The use of antidepressant drugs in the treatment of depression is reviewed. It is suggested that before prescribing antidepressants the physician should: 1) take a detailed history; 2) examine the patient; and 3) evaluate the presenting complaints. Advice on treatment with tricyclic compounds and MAO inhibitors is offered. The role of lithium carbonate in the treatment of bipolar depression is discussed. 10 references.

002950 Kripke, Daniel F.; Simons, Ruth N.; Garfinkel, Lawrence; Hammond, E. Cuyler. Veterans Administration Medical Center (116), 3350 La Jolla Village Dr., San Diego, CA 92161 **Short and long sleep and sleeping pills: is increased mortality associated?** Archives of General Psychiatry. 36(1):103-116, 1979.

Prospective epidemiologic data collected by the American Cancer Society on the relationship between sleeping pills and short and long sleep were analyzed. The data reveal that reported usual sleep durations among groups who complained of insomnia and sleeping pill use often overlapped with those of groups who had no complaints. Reports of insomnia were not consistently associated with increased mortality when several factors were controlled. However, men who reported usually sleeping less than 4 hours were 2.80 times as likely to have died within 6 years as men who reported 7.0to 7.9hours of sleep. The ratio for women was 1.48. Men and women who reported sleeping 10 hours or more had about 1.8times the mortality of those who reported 7.0to 7.9hours of sleep. Those who reported using sleeping pills often had 1.5times the mortality of those who never used sleeping pills. It is concluded that these results do not prove that mortality could be reduced by altering sleep durations or by reducing hypnotic prescribing and that studies are needed to determine the causes of these mortality risk factors. 37 references. (Author abstract modified)

002951 Lader, Malcolm. Department of Psychopharmacology, Institute of Psychiatry, De Crespigny Park, London SE5, England **Psychopharmacology and psychosomatic theory.** Journal of Psychosomatic Research (Oxford). 22(4):299, 1978.

Contents of a paper read at the 21st Annual Conference of the Society for Psychosomatic Research, held in London, November 1977, are reported in a summary. The relationship between psychopharmacology and psychosomatic theory is discussed. Both psychopharmacology and psychosomatics are viewed as suffering from a lack of precision in their concepts, but benefitting from the combination of psychological and pharmacological techniques used in the elucidation of drug effects and disease mechanisms. Although drug studies have inferred that abnormalities involving these amines occur in schizophrenia, it is suggested that such extrapolations are hazardous. The beta-adrenoceptor antagonists used to explore the body/mind relationships implied in some theories of emotion are viewed as more effective in the appropriate psychosomatic condition than are centrally acting tranquilizers. (Author abstract modified)

002952 Leonard, B. E.; Kenny, Marie. Pharmacology Department, University College, Galway, Northern Ireland **Some neuropharmacological aspects of schizophrenia: a short review.** Irish Journal of Medical Science (Dublin). 147(Supplement 1):43-48, 1978.

A paper read at the first Irish Psychopharmacology Conference, held in Belfast in March 1978, is presented. The development of animal models of schizophrenia for the purpose of developing more specific neuroleptics is discussed. The use of amphetamine and apomorphine to initiate stereotypical behavior in rats is described. This method is based on the chronic stimulant model of psychosis. This model is viewed as useful to the study of schizophrenia. The use of hallucinogenic drugs for developing an animal endogenous psychotoxin model of schizophrenia was examined. The use of hallucinogens in animal studies is viewed as having doubtful applicability to schizophrenia research. Although serious objections can be raised to each possible animal model, the chrome amphetamine test appears to be the most useful. 32 references.

002953 Levine, Jerome no address **Contemporary standards for the pharmacotherapy of mental disorders.** Principles and Techniques of Human Research and Therapeutics. Mount Kisco, NY, Futura Publishing, 1978. 292 p. Vol. 2. $16.

Pharmacotherapy is considered in terms of common errors in the treatment of mental disease. Relevant information of proper dosages and expected side-effects for specific classes of drugs is included. Problems in treating specific patient groups, such as children, are also discussed. It is suggested that pharmacotherapeutic agents are not useful in compulsive or addictive disorders in persons with poor impulse control and emotional instability, and in geriatric patients without severe organic impairment.

002954 Lippincott, Richard C.; Hanin, Israel. University of Pittsburgh School of Medicine, Pittsburgh, PA 15260 **The role of contemporary psychopharmacologic agents in the management of pain in dying cancer patients.** Archives of the Foundation of Thanatology. 7(1):37, 1978.

In a summary of a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, pain as a multifactorial and complex perceptual and behavioral concept was discussed. Pain can be evaluated from environmental, physical, and psychological points of view. Areas that need to be reexamined include: the efficacy and ethics of placebo utilization as compared with active psychopharmacologic agents, the role of environment on motivation and subjective pain reporting, and the significance of symptoms of depression. It is concluded that psychopharmacologic interventions alone are not as effective as a multifactorial approach combining all influences known to affect pain perception.

002955 Loo, H. Hopital Sainte-Anne, Faculte Paris-Cochin, 1, rue Cabanis, Paris (14e), France /**Therapeutic disinhibitory agents.**/ Les agents therapeutiques desinhibiteurs. Encephale (Paris). 4(5, Supplement):527-532, 1978.

In a paper presented at the Conference on the Concept of Inhibition in Psychiatry, held in Monastir, Yugoslavia, October 1978, it is suggested that the concept of the disinhibitory agent is heterogeneous. If the disinhibitory property refers to inhibition in its clinical meaning, all psychotropic drugs can be classified as disinhibitory when they are prescribed in some pathological entities. Traditionally, this category refers to a few major tranquillizers, the antipsychotic action of which is linked to the improvement of the affective indifference and of the decrease of the psychomotor activity. However, it is concluded that the pharmacokinetic data reveal that some potent sedative neuroleptics can become disinhibitors at high doses and some disinhibitory agents can become sedative substances at higher doses. 22 references. (Journal abstract modified)

002956 Lowry, Thomas P. Office of Program Review, Department of Developmental Services, Napa State Hospital, Imola, CA **Amyl nitrite: an old high comes back to visit.** Behavioral Medicine. 6(3):19-21, 1979.

Current findings on the use and psychophysiological effects of amyl nitrite are reviewed. The basic pharmacologic action of amyl nitrite is the relaxation of vascular smooth muscle. Amyl nitrite and isobutyl nitrite have become the leading recreational drugs in this country, used to enhance the perception of social activities, particularly sex and dancing. Several studies are discussed, in which no deaths or serious reactions to these drugs were found. Minor complaints are mentioned. 4 references.

002957 Maickel, Roger P. Department of Pharmacology, Medical Sciences Program, Indiana University, Bloomington, IN 47401 **Behavioral pharmacology and therapeutics in the cancer patient.** Archives of the Foundation of Thanatology. 7(1):56, 1978.

In a summary of a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, factors that influence the choice of pharmacologic agents

and type of therapy for the cancer patient were discussed. The use of psychoactive agents in the therapy of the cancer patient represents a very mixed and complex situation. The nature of the specific malignancy, the prognosis for the course of the disease, and the characteristics of the therapeutic processes used to treat the disease are all superimposed upon the personality of the patient and the relationships of the patient to other members of society. It is concluded that there us much more involved than stabilizing the emotional state of the cancer patient.

002958 McCollum, Audrey T.; Margolin, Constance B.; Lieb, Julian. Margolin: Duke University Counseling and Psychological Services, Durham, NC 27706 **Consultation on psychoactive medication.** Health and Social Work. 3(4):71-98, 1978.

The social work clinician's role in prescribing psychoactive medication is discussed. Clinical social workers should be aware of the classes of medication available and of the disorders for which medication may be appropriate. It is suggested that clinicians learn to recognize instances in which they should consider consulting a psychiatrist or other medical professional. The importance of throughly preparing the client for medication is also emphasized. A period of psychotherapy may be necessary before the patient is willing to accept psychoactive drug treatment. It is recommended that the clinician be aware of the complex meanings that the acceptance of medication may have for the patient and develop skill in collaborating with an associate to insure beneficial and comprehensive treatment. 19 references. (Author abstract modified)

002959 McKee, Ian H.; Gill, Cyril. Sighthill Health Centre, Edinburgh, Scotland **Drug treatment of psychiatric patients in general practice.** British Medical Journal (London). No. 6147:1296, 1978.

Tyrer's (1978) study of psychopharmacological treatment of psychiatric patients seen in general practice is critically discussed in two letters to the editor. It is suggested that the study suffers from a number of methodological problems which make his conclusions of frequent misprescribing by general practitioners unwarranted. Small sample size, diagnostic subjectivity, sample bias, and a failure to take human factors into account in prescribing drug regimens are among problems noted.

002960 Mendelson, Wallace B.; Gillin, J. Christian; Wyatt, Richard Jed. Bldg. 10, Room 3N224, National Institutes of Health, Bethesda, MD 20014 **Hypnotics. (Unpublished paper).** Bethesda, MD, NIMH, 1978. 22 p.

The description and classification of hypnotics are examined, as well as complications arising from usage and advice to the physician concerning prescriptions. Addiction as well as deaths from overdose (taken alone or in conjunction with alcohol) are analyzed. It is concluded that the evaluation of relative hypnotic effectiveness is hampered by our poor knowledge of insominia, but that based on our current understanding, no single agent is clearly superior in terms of preserving the normal architecture of sleep. 18 references.

002961 Metzner, Ralph. 707 D Street, Petaluma, CA 94952 **Reflections on LSD -- ten years later.** Journal of Psychedelic Drugs. 10(2):137-140, 1978.

An anecdotal summary of a colloquium in honor of Dr. Albert Hofman, the Swiss chemist who discovered lysergic acid diethylamide (LSD), is presented. Topics of discussion included: the discovery of LSD; politics and LSD, including use by Communist countries and the role of the CIA in LSD research; models of the LSD experience including the psychotomimetic/psychopharmacological, the therapeutic, the psychedelic, and the religious/mystical models; legal and sociocultural aspects of LSD use; and pioneering animal and human LSD research.

002962 Miller, Richard J. Dept. of Pharmacological and Physiological Sciences, University of Chicago, 947 East 58th St., Chicago, IL 60637 **Enkephalin: a peptide with morphine-like properties.** Trends in Neurosciences (Amsterdam). 1(1):29-31, 1978.

Current knowledge of the molecular basis of the action of narcotic drugs is reviewed. The identification of receptors for narcotic drugs in cell membranes from brain and gut and the search for the morphine-like factor, later named enkephalin, which normally acts on these receptors is described. The structure of enkephalin, a peptide, is discussed. The investigation of the localization and function of the opiate peptides through immunohistochemical experiments and radioimmunoassay is presented. The possibility of using this new knowledge to produce new drugs is discussed. 10 references.

002963 Miller, Thomas I. University of Colorado at Boulder **The effects of drug therapy on psychological disorders: a meta-analysis. (Ph.D. dissertation).** Dissertation Abstracts International. 39(5):2511-B, 1978. Ann Arbor, Univ. Microfilms No. 7820540, 225p., 1978.

One hundred forty-eight controlled clinical studies of drug therapy conducted over the last 23 years and representing over 13,000 patients were gathered and their results statistically aggregated. Across all types of patient, research design, and outcome measure, the drug treated patient exhibited more improvement than 70% of control group patients. Results of drug plus psychotherapy are similar to drug therapy alone, with a slight trend suggesting the superiority of drug plus psychotherapy treatment. Patients treated by psychotherapy alone improved signifcantly less than either the drug therapy alone or drug plus psychotherapy treated patients. Chronicaliy ill patients were most aided by drug therapy, and anxious patients showed more improvement than depressed patients. It is concluded that a case can be made for use of meta-analysis in future assessments of drug and drug plus psychotherapy effects, and for less stringent canons for inclusion of studies in future efforts to draw conclusions from large bodies of research. (Journal abstract modified)

002964 Morgan, John P.; Solomon, Joel L. Sophie Davis Center for Biomedical Education, City College of New York,City, New York, NY 10021 **Phencyclidine: clinical pharmacology and toxicity.** New York State Journal of Medicine. 78(13):2035-2038, 1978.

The history, clinical pharmacology, and toxicity of phencyclidine hydrochloride (PCP) are reviewed. Despite effects initially described as unpleasant, PCP has become a very popular street drug. It is easily and inexpensively manufactured and is often misrepresented as THC (tetrahydrocannabinol), psilocybin, mescalin, or other hard to find drugs. Occasionally PCP is contaminated during manufacturing by the toxic byproduct 1-piperidino-cyclohexane-carbonitrile, which may cause abdominal cramps, vomiting, and diarrhea. Neurological effects of PCP itself include ataxia, dysarthria, tremulousness, muscular hypertonicity, and hyperreflexia. The patient may experience paresthesias, analgesia with insouciance to painful stimuli, dystonic posturing or severe dystonic reactions, elevation of systolic and diastolic blood pressure levels, tachycardia, or other arrhythmias. Hallucinations are infrequent and usually involve distention of the body image. Excluding alcohol, PCP is now the most common cause of psychotic, drug related emergency room admission. Information for diagnosis of the syndrome and recommended therapeutic interventions are presented. 10 references.

002965 Murphree, Henry B. Rutgers Medical School, Piscataway, NJ **The use of drugs in the bereaved persons and dying patients.** Archives of the Foundation of Thanatology. 7(1):49, 1978.

In a summary of a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, the use of medications to modify or mitigate signs or symptoms of psychological distress in dying patients and bereaved persons was discussed. Most of the effects of the drugs commonly used by physicians are on emotional states. There are three factors operating in most instances of grief which bear importantly on the use or usefulness of drugs: mastery, adaptive regression, and grief work. Drugs should not be employed in such a way that they interfere with the grief work that the person must do. There is no neat, set formula for using drugs to aid grieving, bereaved, or dying persons. It is concluded that the psychological processes must be assessed in each separate instance, and then an evaluation can be made as to which medication, if any, may be helpful.

002966 no author. no address **Using antidepressants in combination.** Behavioral Medicine. 5(5):44-46, 1978.

The use of MAO inhibitors and tricyclic antidepressants in combination is discussed in terms of the treatment of specific disorders. The patients most likely to respond to combined therapy are those normally diagnosed as having depressive neurosis, particularly those with prominent phobic anxiety, hysteria, and weight loss. Combined therapy has been found especially useful for patients who need an inordinately large amount of tricyclics; are intolerant to therapeutic dosages of tricyclics; have cardiac problems; or cannot afford the tricyclics alone. A sound theoretical rationale for the use of the two classes of antidepressants in combination has been provided by the development of the biogenic amine hypothesis. It is recommended that therapy be approached by administration of a full dosage of one antidepressant initially. If the response is unsatisfactory after a month, the other antidepressant should be gradually added as the initially prescribed drug is gradually withdrawn, until the mood is stabilized. 12 references.

002967 no author. no address **Over-medication renders criminal defendant incompetent to stand trial.** Mental Disability Law Reporter. 2(5):550-551, 1978.

A federal court ruling that the administration of prescribed medication rendered a criminal defendant incompetent to stand trial during a portion of his trial is reported. The court determined that the petitioner, at the time in question, had been drowsy, listless, glassy eyed, not able to stand without staggering, and not able to remain awake at the defense table. The court found that the petitioner had presented substantial facts supporting his contention of incompetence, and that the issue had not been resolved before conviction and sentencing. The court determined that the petitioner had been unable to consult rationally with his lawyer and did not possess the requisite understanding of the proceedings against him.

002968 no author. no address **New Jersey found statutorily authorized to treat involuntary patients without consent.** Mental Disability Law Reporter. 2(4):371, 1978.

A New Jersey state court decision to authorize the administration of Prolixin to involuntarily committed patients without their consent is reported. Although the court acknowledged the plaintiff's reluctance to be treated with Prolixin, and the reasons therefore, it found that the patient's refusal to take Prolixin not to be entirely based on rational considerations, and to reflect delusional thinking. While experimental research, shock treatment, psychosurgery, or sterilization are considered intrusive forms of treatment requiring informed consent, Prolixin was considered commonly employed medical practice. The court noted that until the statute is amended, the only protections afforded involuntarily institutionalized patients will be court review, occasional consultation with an independent expert, and new administrative procedures proposed by the state which will include patient participation in determining treatment plans.

002969 Olsen, Harald; Morland, Jorg. Department of Clinical Pharmacology, University Hospital, Tromso, N-9012, Norway **Ethanol-induced increase in drug acetylation in man and isolated rat liver cells.** British Medical Journal (London). No. 6147:1260-1262, 1978.

The effects of ethanol on drug acetylation was examined in vivo in 16 healthy volunteers and in vitro in isolated rat liver cells. Subjects with a blood ethanol concentration of about 1 g/l were administered oral sulphadimidine. In both rapid and slow acetylators, the apparent half-life of the drug decreased by about 20% after ethanol and the amount of drug acetylated, measured in blood and urine, increased. In three slow acetylators, the ethanol-induced increase was so great that they would otherwise have been classified as rapid acetylators. Suspensions of isolated rat liver cells showed an increase of about 30% in acetylation after addition of ethanol. Results suggest that patients' alcohol consumption should be taken into acount in determinations of acetylator status. The need for further study into the effects of alcohol on drug metabolism is noted. 23 references. (Author abstract modified)

002970 Parker, Richard H. Section of Infectious Diseases, Veterans Administration Hospital, Washington, DC **Drugs, infections, and the dying patient.** Archives of the Foundation of Thanatology. 7(1):28, 1978.

In a summary of a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, 899 May 1978, the effects of psychopharmacologic and analgesic agents on the incidence of infection in the dying patient, and the morbidity caused by the use of antimicrobial agents were discussed. There are few data indicating that either psychopharmacologic or analgesic agents interfere with host immune mechanisms such as phagocytosis, antibody production, or cellular immunity. However, alteration of consciousness by these drugs could make a patient more susceptible to aspiration pneumonia. Side effects of antimicrobial therapy can include discomfort, the development of thrombophlebitis, nausea, vomiting, or diarrhea. It is concluded that before instituting therapy in a dying patient, the potential benefit of such therapy must be weighed against the discomfort.

002971 Perel, James M.; Stiller, Richard L.; Glassman, Alexander H. New York State Psychiatric Institute, Columbia University, New York, NY 10032 **Studies on plasma level/effect relationships in imipramine therapy.** Communications in Psychopharmacology (Oxford). 2(5):429-439, 1978.

At the Symposium on Plasma Level Monitoring of Tricyclic Antidepressants held in Vienna in July 1978, studies showing that the 2-hydroxy metabolites of imipramine (IMI) and desipramine (DMI) are both cardiotoxic and psychoactive in animals and the significance of plasma levels of the drugs were discussed. The relationships between plasma levels and response appears to have been established for imipramine with no apparent indication that high plasma levels were related to paradoxical effects. This linear relationship contrasts with the curvilin-

ear one for nortriptyline. Current issues include clarifications of the relative individual contribution of IMI and DMI, the lack of association between clinical outcome and plasma steady state level of imipramine among unipolar delusional depressive patients, and the role of plasma level monitoring for the treatment of endogenous depression in clinical practice. 31 references. (Author abstract modified)

002972 Plenat, M.; Moulinoux, C.; Coudert, A.-J.; Porot, Maurice. Groupe Hospitalier Saint-Jacques, F-63003 Clermont-Ferrand Cedex, B.P. 69, France **/General anesthesia and long-term psychotropic treatment./** Anesthesie generale et traitements psychotropes au long cours. Encephale (Paris). 4(4):341-348, 1978.

The different attitudes of psychiatrists and anesthetists toward the use of psychotropic drugs before surgery are explored. Anesthetists generally do not distinguish between the various classes of psychotropic drugs. While some of these agents can cause accidents (like MAO inhibitors and reserpine-like agents), others, such as the antidepressants, have no harmful effect. The psychiatric risks when these drugs are removed was reviewed and it is shown that the risks are worth considering. In 8,210 electroshock sessions given under general anesthesia (among which 5,688 were done without removing the psychotropes), there were no cases of severe accidents. 19 references. (Author abstract modified)

002973 Raether, Howard C. National Funeral Directors Association, Milwaukee, WI **I can't believe it!** Archives of the Foundation of Thanatology. 7(1):24, 1978.

In a summary of a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, the pros and cons of the practice of prescribing drugs to help terminally ill patients and their families get over the initial shock of the prognosis were discussed. Frequently today, the reality of a death's impact is amelioriated by various means of denial. One such way is through the prescribing of drugs that cushion the emotional shock and, perhaps, put off the moment of truth so that it may never have to be faced. Death brings problems which must be faced and solved. The pain of loss must be confronted so that it can be healed. It is concluded that the survivors must be helped in their return to normal functioning by means of support systems that give emotional reinforcement and not artificial panaceas.

002974 Reeves, Robert B., Jr. The Presbyterian Hospital in the City of New York, New York, NY **Some reflections on the use of heroin in terminal care.** Archives of the Foundation of Thanatology. 7(1):41, 1978.

In a summary of a paper delivered at a Symposium of the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, some considerations to take into account when making the decision to prescribe heroin or morphine for pain relief in the terminally ill patient were presented. To the degree that the drugs relieve a patient's pain, their effect is good; to the degree that they deprive him of the opportunity to prepare for death, their effect is evil. Either extreme reduces man to something less than fully human. The decision in each case must be particularized. The side effect of morphine is a stupefication; the side effect of heroin is a warping awareness. For some families, blotting out awareness would be preferable to a state of euphoria out of keeping with the patient's character. For others, any retention of awareness, however warped by euphoria, would be preferable to stuperfaction. It is concluded that only when the lifestyle and wishes of the patient and his family are so little known that they cannot be taken into account, should the determination be made mainly on the basis of ease management. 1 reference.

002975 Rose, Marc Richard. University of Denver **Role blurring and social work responsibility: an exploration of social workers' involvement with psychotropic medications. (D.S.W. dissertation).** Dissertation Abstracts International. 39(6):3846-A, 1978. Ann Arbor, Univ. Microfilms No. 7823796. 227 p., 1978.

The extent of social workers' use of psychotropic medications, and its congruence with the perceived responsibilities of social workers was investigated. A sample of 347 social workers completed a questionnaire on attitudes toward social work responsibility, the appropriate role of pharmacotherapy, role blurring, and involvement with psychotropic medications. Involvement with psychotropic medications constituted such activities as self-education, discussions with patients, consultation with and recommendation to M.D.s, participation in the prescribing process, monitoring the effects of medications on patients, and level of knowledge. It was found that while social workers may not be actively prescribing psychotropic medications, they are substantially involved in the remainder of the pharmacotherapeutic process. Furthermore, the workers perceived their involvement as legitimate and well within the responsibilities of the profession. (Journal abstract modified)

002976 Schubert, Daniel S. P.; Miller, Sheldon I. Dept. of Psychiatry, Cleveland Metropolitan General Hospital, 3395 Scranton Road, Cleveland, OH 44109 **Are divided doses of tricyclic antidepressants necessary?** Journal of Nervous and Mental Disease. 166(12):875-877, 1978.

A double-blind, control comparison of the effects of 50mg of clomipramine given three times a day and 150mg of clomipramine in a single bedtime dosage is reported. No significant differences in therapeutic efficacy were found, although patients reported more lightheadedness and dizziness with the single dose. The therapeutic efficacy of the single dose is discussed in relation to the long biological half-life of clomipramine. Advantages of the single dosage include ease of administration, patient compliance, and timing of the sedative effect. 7 references. (Author abstract modified)

002977 Sethi, N. Central Drug Research Institute, Lucknow, India **Psychiatric drugs and teratogenic effects.** Indian Journal of Psychiatry (Poona). 20(4):297-303, 1978.

The teratogenic effects of psychiatric drugs are examined in a review of the literature and available data. The concepts of teratology have widened to include any adverse effect, morphological, biochemical, or behavioral, and induced during fetal life, detected at birth, or later in life. Some of the findings include: chloridiazepoxide, diazepam, and meprobamate have all been reported to produce malformations in the fetus; some tranquilizers show teratogenic potential; no substantial evidence exists that lithium could produce aborrations, even though a few positive cases have been reported; haloperidol needs particular caution; and antidepressants have not yet been studied in as thorough a manner as they deserve. It is concluded that strict caution must be taken when administering psychiatric drugs during pregnancy, especially in the first trimester. 62 references.

002978 Silverstone, Trevor; Turner, Paul. no address **Drug treatment in psychiatry.** 2nd ed. Boston, Routledge & Kegan Paul, 1978. 268 p. $16.75.

An introductory textbook in psychopharmacology is presented in two parts, the first dealing with general principles and the second with clinical applications. The general principle section deals with the history of psychopharmacology, classification and

terminology of psychotropic drugs, neurotransmitters, drug interactions, behavioral effects, and social and psychological aspects of drug treatment. The clinical application section includes discussion of schizophrenia, effective disorders, anxiety, organic psychiatric syndromes, alcoholism, and drug dependency. A brief balanced discussion of all aspects of psychopharmacology is provided.

002979 Simon, Pierre. Dept. de Pharmacologie, Faculte de Medecine Pitie-Salpetriere, 91, boulevard de l'Hopital, F-75634 Paris Cedex 13, France **/Pharmacology and child psychiatry./** Pharmacologie et psychiatrie de l'enfant. Psychiatrie de l'Enfant (Paris). 21(1):319-325, 1978.

The use of psychotropic agents in child psychiatry is examined. The classification of psychotropic drugs is reviewed, and the special problems caused by their administration to children are summarized. Particular emphasis is placed on the rarity and the unsatisfactory nature of therapeutic essays in the domain of child psychiatry, and the reasons for this dilemma are discussed. 3 references.

002980 Simons, Robbi D.; Morris, James L.; Frank, Hugh A.; Green, Linda C.; Malin, Ruth M. Regional Burn Treatmen Center, University of California Medical Center, 225 Dickinson Street, San Diego, CA 92103 **Pain medication contracts for problem patients.** Psychosomatics. 20(2):118, 123, 127, 1979.

The utility of pain medication contracts in aiding communication and reducing power struggles between patients and staff is discussed. Patients' demands for pain medication may arise not only from physical pain but from such sources as fear and anxiety. This in turn creates stress that often leads patients to behave in ways that cause problems for the staff. Manipulative and demanding behavior is extremely common as a response to the feeling of helplessness and loss of control and to generalized anxiety. It is suggested that good candidates for pain contracts include patients whose lifestyles are characterized by contention for control such as drug addicts, patients with passive/aggressive personality, and neurotics. 4 references.

002981 Soldatos, Constantin R.; Kales, Anthony; Cadieux, Roger. Sleep Research and Treatment Center, Pennsylvania State University College of Medicine, Hershey, PA 17033 **Narcolepsy: evaluation and treatment.** Journal of Psychedelic Drugs. 10(4):319-325, 1978.

Symptoms indicating a diagnosis of narcolepsy are described and the treatment of the disorder is discussed. Narcolepsy is estimated to afflict between .02 and .07% of the general population. Criterion for diagnosis is the presence of one or more of the symptoms of the narcoleptic tetrad: sleep attacks, cataplexy, sleep paralysis, and hypnagogic hallucinations. Laboratory and clinical findings indicate that certain manifestations of the auxiliary symptoms of narcolepsy are related to the neurophysiological mechanisms of REM sleep. Pharmacological management of narcolepsy entails separate treatments for the sleep attacks and the auxiliary symptoms. Initial treatment of the most troublesome symptom is recommended. It is recommended that: therapeutic naps be utilized wherever possible, the lowest effective dose of medication be administered, medication be administered early in the day, patients be carefully monitored during combined drug therapy, and the psychosocial consequences of the disorder not be neglected. 28 references.

002982 Stillman, Richard C.; Willette, Robert E. Division of Research, National Institute on Drug Abuse, Rockville, MD 20857 **The psychopharmacology of hallucinogens.** New York, Pergamon, 1978. 338 p. $32.50.

Papers read at the workshop assessing hallucinogenic behavior sponsored by the Division of Research of the National Institute on Drug Abuse in Bethesda, Maryland, December 1976, are presented. The mechanisms of action of hallucinogenic drugs are explored by considering the methodology for assessing hallucinogenic behavior, by developing models for the effects of hallucinogens on animal and human behavior, and by correlating the molecular structure of these compounds with consequent behavior. Topics include: biosynthesis and action of hallucinogens; biogenic amines; molecular mechanism of action; molecular determinants for interaction with the lysergic acid diethylamide (LSD) receptor; a receptor model for hallucinogenic amphetamines; psychotomimetics; phencyclidine; LSD-like hallucinogens; N,N-dimethyltryptamine; mescaline; unconditioned and conditioned behaviors in evaluating possible hallucinogenic agents; Pavlovian conditioning; an animal behavior model for studying the action of LSD and related hallucinogens; behavioral measures of hallucinogenic behavior; animal models of drug-induced hallucinations; attentional dysfunction; euphorohallucinogens; and the chemical transcendental state.

002983 Stoff, David M.; Gillin, J. Christian; Wyatt, Richard Jed. Saint Elizabeths Hospital, Washington, DC 20032 **Animal models of drug-induced hallucinations.** In: Stillman, R., The psychopharmacology of hallucinogens. New York, Pergamon, 1978. 338 p. (p. 259-267).

A paper read at the workshop on assessing hallucinogenic behavior sponsored by the Division of Research of the National Institute on Drug Abuse in Bethesda, Maryland, December 1976, is presented. The relationship between the effects of hallucinogenic drugs in animals and humans on a correlational or inferential basis is explored. Topics discussed include: problems in developing animal models of drug-induced hallucinations, animal models of human psychological states, analogue or assay models, criteria for an animal model of hallucination, and the development of animal models. It is proposed that the main value of animal screening procedures is to predict activity of potential hallucinogenic drugs and their potency. 23 references.

002984 Strayhorn, Joseph M.; Nash, James L. Dept. of Psychiatry, Duke University Medical Center, Durham, NC 27710 **Frightening dreams and dosage schedule of tricyclic and neuroleptic drugs.** Journal of Nervous and Mental Disease. 166(12):878-880, 1978.

To investigate the relationship between dosage schedule of tricyclic and neuroleptic drugs and frequency of frightening dreams, and to see whether differences in frequency of frightening dreams were a function of differences in total dream recall, a questionnaire was administered to 91 outpatients in a Veterans Administration mental hygiene clinic, asking about frequency of dream recall, frequency of frightening dream recall, and doses and times of any medications taken. More frequent frightening dreams in patients on bedtime only dosage schedules were found, but no significant difference between the two groups with respect to frequency of dream recall. 5 references. (Author abstract modified)

002985 Stunkard, Albert J. Dept. of Psychiatry, University of Pennsylvania, Philadelphia, PA 19104 **The development of tolerance to appetite suppressant medication: new theory, new hope.** Journal of Psychedelic Drugs. 10(4):331-341, 1978.

A new theory of tolerance to appetite suppressant medication is presented. It is argued that traditional views of the method of action of appetite suppressant medication do not adequately encompass newer findings on the regulation of bodyweight. The proposed theory states that the effectiveness of appetite suppressant medication depends upon the nutritional state of the orga-

nism, and that the medications act by lowering the level about which the bodyweight and particularly body fat are regulated. The action of these drugs upon appetite and food intake is secondary to the establishment of lower levels of body fat. It is greatest at higher levels of body fat and decreases in proportion to falling levels of body fat. Data are presented from a recent study of fenfluramine which supports the view that tolerance to this medication, as traditionally defined, does not develop. 16 references.

002986 Tsunenari, Shigeyuki; Shimoda, Ryoichi; Kanda, Mizuho; Muto, Hitoshi; Takahama, Keiichi. Dept. of Legal Medicine, Kumamoto University Medical School, Kumamoto, Japan **Forensic chemical determinations of ""Nervenruh-forte (Neuron-forte)", crude drug tranquilizer.** Japanese Journal of Legal Medicine (Tokyo). 32(1):21-25, 1978.

Qualitative determination of an unknown tranquilizer was carried out on test samples obtained at the autopsy done on a 41-year-old female by thin layer chromatography (TLC) and ultraviolet spectrophotometry (UV). The main constituents of ""nervenruh-forte" in gastric contents, liver, brain, and blood were extracted and analyzed. Water soluble vehicle and crude drugs in the tranquilizer were detected by four systems of TLC. The blood sample was found by UV to have the maximum absorption at 330 millimicrons, which was derived from the absorption spectrum of the tannin-like substances in the substance. It is crucial for the forensic chemical identification of pharmacognostic drugs to set up an analytical target, because every crude drug has many constituents, such as alkaloids, flavonoids, essential oils, and tannins. 10 references. (Journal abstract modified)

002987 Tyler, G. Scott. no address **Post head injury syndrome.** Trial. 14(3):33-35, 1978.

The posthead injury (triad of headache, dizziness and personality change) syndrome is illustrated by two case reports, and the use of tricyclic antidepressants for the treatment of posthead injury syndrome is described. In posthead injury syndrome, the patient and everyone in his or her environment, spouse, children, employer, physician, and attorney must deal with a painful and seemingly hopeless situation. Every force must be mobilized and mutually renewed to avoid the social and financial fatality of the patient giving up his battle. While the posthead injury personality change involves much more than depression, and while the accompanying headache is not necessarily vascular in nature (posthead injury headache can be divided into vascular, muscle tension strain, peripheral neuroma, and nonspecific types), a trial of tricyclic antidepressants is recommended. The initial beneficial result will almost always wane at which time the dosage must be increased. Such waning is concomitant with a decrease in the dryness of the mouth that invariably accompanies the therapeutic effect.

002988 Ungerleider, J. Thomas. Dept. of Psychiatry, UCLA, Los Angeles, CA 90024 **Less common uses of amphetamines.** Journal of Psychedelic Drugs. 10(4):327-329, 1978.

Uses of amphetamines discussed in the medical literature, but not listed in the Physician's Desk Reference, are reviewed. Over 100 uses of amphetamines have been mentioned in the published medical literature. These include use in the treatment of: migraine, morphine withdrawal, pulmonary tuberculosis, acute barbiturate poisoning, prepartum nausea and vomiting, paroxysmal hiccough, hayfever symptoms, spasm of the gastrointestinal tract, irradiation sickness, epilepsy, spasmatic flexion of the foot, myasthenia gravis, postencephalitic parkinsonism, war neuroses, heart block, dizziness, enuresis, codeine addiction and withdrawal, myotonia, and oculogyric crises in parkinsonism. The use of amphetamine in the treatment of depression, pain, and epilespy is discussed in depth. 23 references.

002989 van der Kolk, Bessel A. 30 Braddock Park, Boston, MA 02116 **Organic problems in the aged: brain syndromes and alcoholism -- discussion.** Journal of Geriatric Psychiatry. 11(2):167-170, 1978.

Comments regarding a paper delivered by Thomas Ban to the Seventeenth Annual Meeting of the Boston Society for Gerontological Psychiatry, dealing with organic brain problems in the elderly, are presented. It is noted that, even if a greater understanding of the causes, pathophysiology, and biochemistry of senile dementia were to be reached, therapeutic progress would not inevitably follow. The morphological changes underlying senile dementia are irreversible. The management of persons with the disorder, however, has made tremendous progress. With the introduction of antipsychotic agents, paranoia and agitation can be controlled, and patients can be reintegrated with their environments. The role of a stable environment in decreasing anxiety is noted. The overuse of psychotropic medications in the treatment of senile dementia is discussed. 1 references.

002990 Van Putten, Theodore; May, Philip R. A.; Marder, Stephen R. Veterans Administration Hospital, Wilshire and Sawtelle Blvds., Los Angeles, CA 90073 **The hospital and optimal chemotherapy in schizophrenia.** Hospital & Community Psychiatry. 30(2):114-117, 1979.

The need for hospitalization of schizophrenics receiving chemotherapy is discussed. It is stated that in some cases, chemotherapy of schizophrenics is best monitored in a hospital setting. Dysphoric responders and noncompliers are identified as patients who can most benefit from monitoring in the hospital. Dysphoric responders, whose illnesses have been only minimally responsive to antipsychotic drugs, are in danger of psychotoxicity due to excessive dosage. Habitual noncompliers have little investment in staying well and are unlikely to bear even mild drug side-effects. The use of the test dose concept to monitor drug response is described. 42 references. (Author abstract modified)

002991 Vener, Arthur M.; Krupka, Lawrence R.; Climo, Jacob J. Dept. of Social Science, Michigan State University, Bessey Hall, East Lansing, MI 48824 **Drug usage and health characteristics in noninstitutional retired persons.** Journal of the American Geriatrics Society. 27(2):83-90, 1979.

Total drug usage (prescription, over the counter, social), health characteristics, and life satisfaction were studied in 55 noninstitutional retired men and women whose average age was 70 years. The sample was purposively selected on the basis of involvement in peer group interaction networks. Among those using drugs, the average number taken per person was 2.0prescription, 1.8over the counter, and 1.8social (alcohol, caffein, nicotine). The average for men was 7.5and 4.7drugs for women. Although drug interaction hazards from prescription drugs alone appeared to be minimal, examination of total drug usage indicates potential interactive hazards. Despite the number of chronic illnesses, physical impairments, and the number of drugs ingested, the respondents usually expressed overall satisfaction with their life condition. Respondents had confidence in both their physicians' diagnoses and the effectiveness of the drugs prescribed. Women reported more chronic diseases and physical impairments and were relatively more dissatisfied with their life condition than were men. It is suggested that this may be associated with their greater acquiescence with self-disclosure. 33 references. (Author abstract modified)

002992 Wolf, Stewart G., Jr. St. Luke's Hospital, Bethlehem, PA **Choosing chemotherapy for pain and suffering in the dying**

patient and the bereaved. Archives of the Foundation of Thanatology. 7(1):31, 1978.

In a summary of a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, the factors involved in choosing chemotherapy for pain and suffering in the dying patient were discussed. A physican should tailor all decisions as to supports and drugs to be used to the needs and desires of the individual to be treated. The coping strategies of individuals differ from one another. Usually the relief of pain, anxiety, and tension is appropriate. Alcohol, morphine, and heroin are reliable agents. There is a place for the newer psychotropic drugs especially when attacking specific symptoms such as depression, intense anxiety, or an obsessive, ruminative tension state. Barbiturates are helpful when it is appropriate for people to be rendered unconscious.

002993 Wolff, B. Berthold. New York University Medical Center, New York, NY 10003 **Use of analgesic agents in the clinical and psychosocial care of the dying patient.** Archives of the Foundation of Thanatology. 7(1):38, 1978.

In a summary of a paper delivered at a Symposium on the Use of Psychopharmacologic and Analgesic Agents in the Clinical and Psychosocial Care of the Dying and Bereaved held at the Columbia-Presbyterian Medical Center, New York, May 1978, alternatives to potent narcotics to control or manage chronic pain in the dying patient were discussed. The question is raised as to whether it is ethical and humane to dope the dying patient to such an extent that he is no longer a proper functional human being psychologically. A differentiation is made between acute and chronic pain, chronic pain requiring different therapeutic approaches. Pain therapeutic modalities include: pharmacologic, nonablative physical, surgery, and behavioral. Therapeutic modalities have to be custom made for the individual patient, but usually a combination of pharmacologic or physical modalities combined with a psychological modality appear to be the most effective. It is concluded that it is possible to control even severe chronic pain effectively with relatively mild analgesic therapies, and to let the dying patient continue to function as a responsible, psychologically intact individual without doping him.

002994 Yesavage, Jerome A. Stanford University School of Medicine, Stanford, CA 94305 **Practical points in using dihydroergotoxine mesylate (Hydergine) in senile dementia.** Psychiatric Annals. 8(9):74-75, 79, 83, 1978.

The importance of patient selection, research methodology for the clinical trial, and appropriate drug dosage in the use of dihydroergotoxine mesylate (Hydergine) in senile dementia are described. Since many conditions can mimic the signs and symptoms of senile dementia, it is necessary to carefully rule out other, similar conditions. The use of the Hamilton depression rating scale as part of a complete neuromedical work up, and use of the Crichton Royal Behavioural Rating Scale and the Sandoz Clinical Assessment Geriatric scale as premedication baseline measures are recommended. It is concluded that Hydergine may have a long-term prophylactic effect on the patient even if there is little or no improvement in his condition. 7 references.

002995 Zawadski, Rick T.; Glazer, Gerald B.; Lurie, Elinore. On Lok Senior Health Services, 1490 Mason Street, San Francisco, CA 94133 **Psychotropic drug use among institutionalized and noninstitutionalized Medicaid aged in California.** Journal of Gerontology. 33(6):825-834, 1978.

The California Medicaid data base is used to compare the amount and pattern of prescription drug use among the aged to that of the general population, and then compares, within the aged population, drug use by the institutionalized and noninstitutionalized. It was found that prescription drug use was higher for the aged as compared to the general population, thus confirming the findings of previous research. Among the aged, however, prescription drug expenditures were almost three times as high for the institutionalized as compared to the noninstitutionalized. The bulk of the difference in prescription drug expenditure among the aged subgroup was found to be due to a much higher level of psychotropic drug use among the institutionalized. Data from a sample of aged in a day health program raises questions about the appropriateness of this level of psychotropic drug use. 15 references. (Author abstract modified)

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